United States Court of Appeals

for the Second Circuit

APPENDIX

74-1738

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P/S

In The

United States Court of Appeals

For The Second Circuit

THE NATIONAL NUTRITIONAL FOODS ASSOCIATION, and SOLGAR, CO., INC.,

Plaintiffs-Appellants,

vs.

CASPER W. WEINBERGER, Secretary of Health Education and Welfare and ALEXANDER M. SCHMIDT, Commissioner of Food and Drugs,

Defendants-Appellees.

On Appeal from the United States District Court for the Southern District of New York.

JOINT APPENDIX

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UNITED STATES COURT OF APPEALS
FILED
AUG 7 1974
A. DANIEL FUSARO, CLERK
SECOND CIRCUIT

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DOCKET ENTRIES

The National Nutritional Foods Et.ano. v Caspar W. Weinberger JUDGE F

73 Civ.

A TRUE COPY
RAYMOND F. BURGHARDT, Clerk
By
Deputy Clerk

	PROCEEDINGS
[illegible]-73	Filed complaint and issued summons
[illegible]-73	Filed pltff's affdvt. & notice of motion for preliminary injunction
[illegible]-73	Filed pltff's memorandum of law in support of pltff's motion for injunction
[illegible]-73	Filed defts Order to Show Cause: Re: Adjourn Preliminary Injunction.-ret. Frankel in room 128 or to such other time and place J. Frankel may fix. So Ordered, M
Aug 17-73	Filed summons with marshals return, Served Lasper W. Inberger Sec. H.E.W. etc. also served Alexander M. Schmidt, Comm. of FDA on 8-9-73.
Sept. 10-73	Filed certificate of Alexander M. Schmidt, M.D. re: 45 volumes of documents.
Sept. 10-73	Filed Govt's notice of motion re: dismissal before Frankel J. on 9-17-73
Sept. 10-73	Filed deft's Memo in opposition to pltff's motion for a preliminary injunction and in support of deft's motion to dismiss.
Sept. 10-73	Filed appendix to deft's Memorandum of Law.
Sept 12-73	Filed affidavit of Joseph John Vitale.
Sept 12-73	Filed reply memorandum in support of pltffs motion for a preliminary injunction
Sept 17-73	Filed pltffs supplemental memorandum.
Sept 17-73	Filed pltffs supplemental appendix.
Sept 20-73	Filed affdvt. of Naomi L. Reice, AUSA, dated 9-19-73.
Sept. 20-73	Filed deft's memorandum in response to pltff's supplemental memorandum.
Sept.25-73	Filed Memorandum-Opinion # 39849--in short, the public interest in healthfuit overwhelms the financial concerns plaintffs urge-beyond that, the likelihood that pltffs. will succeed in this action seems negligible- there are, then, no grounds for, and powerful grounds against, a preliminary injunction. pltff's motion is denied. So ordered FRANKEL, J.
Sept25-73	Filed pltff's notice of appeal to USCA from order denying pltff's motion for preliminary injunction entered 9-25-73. Mailed copy to:USA SDNY
Oct.2-73	Filed certification of record on appeal.
Oct 5-73	Filed pltffs notice to take deposition of A. M. Schmidt. on 10-15-73.
Oct.15-73	Filed defts order and order to show cause why an order should not be entered pursuant to rule 26(c)vacating a notice of deposition..Ordered that pltff is restrained from taking deposition of deft Alexander M. Schmidt..Ret.10-26-73 9:30a
Oct.25-73	Filed pltffs.' affdvt. by Milton A. Bass in opposition to defts' motion to vacate as indicated.
Nov. 9-73	Filed stip & order that oral argument on defts' motion to quash the deposition notice for Alexander M. Schmidt is adjourned until a mutually convenient date following a decision by the Court of Appeals as indicated. So ordered FRANKEL, J.
Dec. 5-73	Filed transcript of proceedings of 9-13-73
Dec.13-73	Filed affdvt. of Naomi L.Reice,AUSA & Exhibits (Vols. I & II)attached.
Dec.26-73	Filed supplemental affdvt.in opposition to defts motion to vacate notice of deposition.
Jan. 9-74	Filed defts' supplemental memorandum.
Feb.7-74	Filed pltffs' Memorandum of Law in opposition to defts' motions for summary judgment and to vacate the notice of deposition.
Feb.14-74	Filed true copy of USCA mandate with opinion attached- order of District Court is affirmed with costs to be taxed against the appellants in the sum of $ 598.37 - Docketed as Judgment #74,187 on 2-19-74
April 5-74	Filed Opinion # 40555- on 10-1-73, regulations of the Food and Drug Administration became effective requiring that preparations of Vitamin A and Vitamin as indicated be restricted to prescription sale and that such vitamins be labeled accordingly. Pltffs., involved in the manufacture, distribution, and sale of Vitamin A and D, filed suit on 8-6-73, seeking declaratory and injunctive relief against the regulations.
[illegible]-5-74	(Cont'd) -- Opinion # 40555----defts. have now moved for summary judgment dismissing the complaint. The reasons are stated in opinion- pltffs' notice of deposition is vacated, defts' motion for summary judgment is granted. The complaint is dismissed. So ordered- FRANKEL, J. (m/n)
[illegible]-6-74	Filed Judgment- ordered that defts. Caspar W. Weinberger, Secretary of H.E.W. Alexander M. Schmidt, Commissioner of Food & Drugs, have judgment against the pltff. The National Nutritional Foods Association and Solgar Co., Inc. dismissing the complaint. Clerk (m/n)
May 16-74	Filed pltffs notice of appeal from the final order dismissing the complaint, entered on 4-6-74. Copy mailed to: U.S. Atty. Entered 5-17-74

COMPLAINT

UNITED STATES DISTRICT COURT (Filed August 6, 1973)
SOUTHERN DISTRICT OF NEW YORK

----------x

THE NATIONAL NUTRITIONAL FOODS ASSOCIATION and SOLGAR CO., INC.,

Plaintiffs,

-against-

COMPLAINT

CASPER W. WEINBERGER, Secretary of Health, Education and Welfare and ALEXANDER M. SCHMIDT, Commissioner of Food and Drugs,

Defendants.

----------x

STATEMENT AS TO JURISDICTION AND VENUE

1. This is an action for (a) a declaratory judgment that the provisions of the regulations entitled "Vitamin A Preparations for Oral Use as Drugs" and "Vitamin D Preparations for Oral Use as Drugs" at 21 CFR §§3.94 and 3.95 published in the Federal Register on August 2, 1973 at 38 F.R. 20723-20725 (hereinafter referred to as the "Vitamin A and D Regulations"), are not in accordance with law, are in excess of the statutory jurisdiction, authority and limitations of the defendants and are short of statutory right, and (b) for injunctive and other relief.

2. Jurisdiction of this Court is invoked pursuant to 28 U.S.C. §§1331(a) and 1337. The matter in controversy exceeds the sum or value of $10,000.00, exclusive of interest and costs, and the action arises under the laws of the United States, namely the Federal Food, Drug and Cosmetic Act, 21 U.S.C. §301 et seq.

and also the Administrative Procedure Act, 5 U.S.C. §1001 et seq.

3. This action is authorized by 28 U.S.C. §§2201 and 2202 and 5 U.S.C. §1009. The plaintiffs are suffering legal wrong because of the final agency action of the Commissioner of Food and Drugs in promulgating the Vitamin A and D regulations and are aggrieved by such action. This is a case of actual controversy which requires a declaration with respect to the invalidity of said regulations as alleged in this complaint.

4. Venue in this judicial district is proper by virtue of 28 U.S.C. §1391(e)4.

PARTIES

5. Plaintiff Solgar Co., Inc. is a New York corporation with its principal place of business in this district at 92 East 10th Street, New York, New York, and engages in the manufacture, distribution and sale in interstate commerce of vitamins and dietary supplements. Plaintiff National Nutritional Foods Association is composed of business concerns located in New York State and throughout the United States, including manufacturers, wholesalers and retailers of vitamins and dietary supplements. The plaintiffs join as such in this one action since they assert rights to relief in respect of and arising out of the same transaction and occurrence and questions of law common to both of them will arise in this action.

6. Defendant Casper W. Weinberger is the Secretary of Health, Education and Welfare and is the officer charged with the administration of the Federal Food, Drug, and Cosmetic Act. He is authorized by 21 U.S.C. §371 to promulgate regulations for

the efficient enforcement of the Act. Defendant Alexander Schmidt is the Commissioner of Food and Drugs and is responsible for the supervision of the Food and Drug Administration. The Secretary of Health, Education and Welfare has purported to assign to the Commissioner of Food and Drugs the functions vested in the Secretary under the Federal Food, Drug and Cosmetic Act. The defendant Commissioner is the officer who, purportedly under color of legal authority, promulgated the Vitamin A and D regulations.

FACTUAL ALLEGATIONS

7. The Vitamin A and D regulations promulgated by the defendant Commissioner declare that preparations which contain Vitamin A in excess of 10,000 International Units per dosage unit are drugs and limit such items to sale by prescription only. The same limitations are applied to preparations containing Vitamin D in excess of 400 International Units per dosage unit. Preparations labeled contrary to the regulations are made subject to regulatory proceedings as of October 1, 1973.

8. The Commissioner of Food and Drugs set forth the purported rationale for the above limitations at 37 Federal Register 26618-26620, December 14, 1972, by asserting that toxicity of Vitamins A and D at high levels required the dosage limitations and classifications as ultimately promulgated in the Vitamin A and D regulations. As scientific support for his position, the Commissioner cited supposed scientific information and literature regarding Vitamin A and D toxicity which had been listed with the Hearing Clerk of the Department of Health, Education and Welfare.

9. The body of scientific knowledge relating to Vitamin A

and D toxicity absolutely demonstrates that the dosage limitations and classifications in the Vitamin A and D regulations are totally without scientific foundation or merit. Neither the general body of scientific knowledge nor the literature cited by the Commissioner provide any factual or medical basis for the promulgation of the Vitamin A and D regulations. These regulations are arbitrary, unjust, an abuse of the regulatory power prescribed by Congress and beyond the legal authority of the Commissioner of Food and Drugs and the Secretary of Health, Education and Welfare.

10. The provisions of the Vitamin A and D regulations are additionally beyond the scope of any legal authority in that they arbitrarily and without any statutory authority classify certain common food items as drugs and arbitrarily and without statutory authority require them to be dispensed only by prescription.

11. The promulgation of the Vitamin A and D regulations is additionally beyond the scope of any legal authority in that they involve questions of scientific and medical knowledge and facts which were decided unilaterally and arbitrarily by the defendant Commissioner without any public hearings wherein competent testimony could have been adduced to determine such factual questions in accordance with due process of law.

12. Plaintiff Solgar Co., Inc. and the members of plaintiff National Nutritional Foods Association are aggrieved by the promulgation of the Vitamin A and D regulations in that their manufacture, distribution and sale of products containing Vitamin A and D will be unnecessarily and unlawfully restricted

to a very large degree by the requirement of sale by prescription at the specified dosage levels. Plaintiffs are presently aggrieved and injured by the Vitamin A and D regulations in that their production, distribution and inventory patterns are immediately affected. The enforcement of the Vitamin A and D regulations after October 1, 1973 , even for a temporary period during the pendency of this action, will cause great and irreparable damage to plaintiffs from the nationwide loss of sales on their Vitamin A and D products.

13. Plaintiffs have no prompt, adequate and effective remedy at law, and this action is the only means available to them for the protection of their rights and for the protection against the immediate, real and substantial damage and injury which plaintiffs face.

WHEREFORE, Plaintiffs pray that this Court:

(1) Issue a judgment declaring that the Vitamin A and D regulations are not in accordance with law, are in excess of statutory jurisdiction, authority and limitations of the defendants, and contrary to the statutory provisions on which they purport to be based, and are null and void and of no effect.

(2) Enjoin and restrain the defendants and all persons acting under their direction and authority, or in active concert or participation with them, from enforcing or causing to be enforced, or from attempting to enforce or to cause to be enforced, by any administrative action or civil or criminal proceeding, the Vitamin A and D regulations alleged herein as being null and void

and of no effect.

(3) Issue a preliminary injunction enjoining and restraining the defendants and said other persons from enforcing or causing to be enforced or attempting to enforce or to cause to be enforced, by any administrative action or civil or criminal proceeding or otherwise, said provisions of the Vitamin A and D regulations and to preserve the status and rights of plaintiffs pending conclusion of this action.

(4) Grant such other and further necessary or proper relief as to this Court may seem just and proper.

Dated: New York, New York
August 6, 1973

BASS & ULLMAN

By: _____
(A Member of the Firm)

Office & P.O. Address
342 Madison Avenue
New York, New York 10017
(212) 697-3880

UNITED STATES DISTRICT COURT (Filed August 15, 1973)
SOUTHERN DISTRICT OF NEW YORK

THE NATIONAL NUTRITIONAL FOODS ASSOCIATION and SOLGAR CO., INC.,

Plaintiffs,

-against-

CASPER W. WEINBERGER, Secretary of Health, Education and Welfare, and ALEXANDER M. SCHMIDT, Commissioner of Food and Drugs,

Defendants.

Index No. 73 Civ. 3448

MOTION FOR PRELIMINARY INJUNCTION

Upon the complaint herein and the annexed affidavits of Robert Ullman, Harold Rosenberg, D.O., Carlton Fredericks, Allen Skolnick and Philip Pollack, and upon the Agriculture Handbook No. 8 prepared by the Agricultural Research Service, U.S.D.A., entitled Composition of Foods, plaintiff will move this Court on August 27th, 1973 for a preliminary injunction enjoining the defendants herein, their agents, servants, employees and attorneys and all persons in active concert and participation with them, from enforcing or causing to be enforced, or attempting to enforce or to cause to be enforced, the "Vitamin A and D Regulations" at issue herein, on the grounds that

(1) Unless restrained by this court defendant will perform the acts referred to;

(2) Such action by the defendant will result in irreparable injury, loss and damage to the plaintiffs, as more particularly appears in the complaint and the affidavits of Allen Skolnick and Philip Pollack, attached hereto;

(3) The issuance of a preliminary injunction herein

will not cause undue inconvenience, loss or injury to defendant, or to the public, but will prevent irreparable injury to plaintiffs.

Dated: New York, New York
August 15, 1973

BASS & ULLMAN

Attorneys for Plaintiffs
Office & P.O. Address
342 Madison Avenue
New York, New York
(212) 697-3880

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

(Filed August 15, 1973)

THE NATIONAL NUTRITIONAL FOODS ASSOCIATION and SOLGAR CO., INC.,

Plaintiffs,

-against-

CASPER W. WEINBERGER, Secretary of Health, Education and Welfare, and ALEXANDER M. SCHMIDT, Commissioner of Food and Drugs,

Defendants.

Index No. 73 Civ. 3448

AFFIDAVIT

STATE OF NEW YORK)
) SS.:
COUNTY OF NEW YORK)

ALLEN SKOLNICK, being duly sworn, deposes and says:

1. I am the Vice-President of plaintiff Solgar Co., Inc. which is a member of the plaintiff National Nutritional Foods Association, and I make this affidavit in support of plaintiffs' motion for preliminary injunction restraining the defendants herein from enforcing the order published in the Federal Register at 38 F.R. 20723-20725, known as the "Vitamin A and D Regulations."

2. For the past 26 years, Solgar Co., Inc. has been engaged in the formulation, packaging, distribution and sale of various vitamin and dietary food supplement products. Our products are sold nationwide both under our own and under private label and the current annual volume of our sales is approximately two million dollars. Other members of the NNFA, located through-

out the United States, are similarly engaged in such activities at the manufacturer, wholesaler, distributor, and retailer levels.

3. The Vitamin A and D regulations promulgated by the defendant Commissioner of Food and Drugs, declare that any product containing more than 10,000 I.U. of Vitamin A per dosage unit and more than 400 I.U. of Vitamin D per dosage unit, are drugs which may be purchased by the consumer only by prescription.

4. Solgar Co., Inc. is currently distributing approximately 150 products containing Vitamin A and/or Vitamin D which are affected by the new regulations. Our annual sales of these products total approximately three quarters of a million dollars, accounting for approximately 40 percent of our total sales.

5. The new regulations have already wrought total havoc with our company's current production, distribution and inventory planning. After October 1, 1973, the Vitamin A and D regulations will prohibit us from continuing to manufacture, label, and ship in interstate commerce the variety of products mentioned above without drastically changing their composition. In addition, all of our advertising, promotional and informational material and literature will have to be discarded and revised in order to advise the customer that he will no longer be getting the dosages presently found in our products. Thus, at the very outset we will immediately be faced with relabeling and reformulation costs totaling in the area of $50,000 in order to make the above changes. It is clear to us that if the Vitamin A and D regulations are enforced, our company faces the loss of

a substantial portion of the $750,000 sales of products containing Vitamin A and D. Moreover, the reputation, good will and integrity established by the sale of our products for over 20 years will immediately be thrown into question by the sudden forced change in formulation. The effect of the instant regulation would be to jeopardize our entire product line by imposing new restrictions and creating totally new marketing conditions which are completely out of line with reality.

6. The FDA claims of health hazards with respect to the current Vitamin A and D dosages available in the marketplace are contradicted by our marketing experience. Although some of our products contain dosages of Vitamin A in excess of 10,000 I.U. and Vitamin D in excess of 400 I.U., we have never received any report of adverse effects from the use of our products. These types of products and dosages have been on the market for over 30 years and have been used by millions of consumers. I respectfully request that in order to maintain the status quo and to avoid the irreparable injury to our company as outlined above, the defendants in this case be preliminarily enjoined from enforcing the Vitamin A and D regulations so that the plaintiffs herein can have an effective remedy upon their presentation to the court of evidence demonstrating that the new regulations are medically, scientifically and factually unsound and unreasonable, as well as beyond the scope of the authority of the Commissioner of Food and Drugs.

ALLEN SKOLNICK

Sworn to before me this

day of August, 1973.

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

(Filed August 15, 1973)

THE NATIONAL NUTRITIONAL FOODS ASSOCIATION and SOLGAR CO., INC.,

Plaintiffs,

-against-

CASPER W. WEINBERGER, Secretary of Health, Education and Welfare, and ALEXANDER M. SCHMIDT, Commissioner of Food and Drugs,

Defendants.

Index No. 73 Civ. 3448

AFFIDAVIT

STATE OF NEW JERSEY)
) SS.:
COUNTY OF BERGEN)

PHILIP POLLACK, being duly sworn, deposes and says:

I am the President of Leeds-Dixon Laboratories Corp., Moonachie, New Jersey. Leeds-Dixon is a member of plaintiff National Nutritional Foods Association and is a wholly owned subsidiary of Iroquois Brands, Ltd., a New York corporation whose stock is publicly held.

Leeds-Dixon is a manufacturer and distributor of a variety of products, including dietary supplements of vitamins and minerals under the trade names Schiff Bio Foods, Basic Organics and Natura Brands. This vitamin business was started by Eugene Schiff over 25 years ago. Today our products are sold on a nationwide basis. In addition to manufacturing vitamin products under our own labels, we manufacturer and package formulations under private label for distribution throughout the country, primarily in retail Health Food Stores, and we further

manufacture and sell in bulk vitamin and mineral products for repackaging and sale by other companies.

Considering our own label products, private label products, and bulk sales, the formulations we manufacture and sell include Vitamin A and D in over 450 products. I would estimate the gross annual sales of such products to be in excess of one million dollars.

On August 2, 1973, the Food and Drug Administration published regulations which for the first time in our more than twenty-five years in business would allow products containing more than 10,000 I.U. Vitamin A and 400 I.U. Vitamin D to be sold on prescription only. All products labeled after October 1, 1973 are required to be in compliance with these regulations. An immediate consequence of such regulations would be that products which we have sold for as long as twenty-five years as dietary food supplements would have to be either discontinued or reformulated; advertising, product labels, catalogs and other labeling and promotional material currently being used would have to be discarded and revised; we could no longer manufacture food supplements containing Vitamins A and D at levels in excess of 10,000 I.U. and 400 I.U. respectively; our customers and their customers in turn, would no longer be able to buy from us food supplements of their choice containing Vitamins A and D beyond the levels of 10,000 I.U. and 400 I.U. although they have been purchasing such products in the past without such restriction, in some instances as long as twenty-five years and even longer.

In addition to this effect on the products we sell,

there will be an immediate disruption of our production planning and manufacturing schedules. This sudden changeover will require new manufacture and new labeling of revised formulations after October 1, 1973. I would estimate that we will have to expend over $75,000 almost immediately, to change labels, formulae, catalogs, etc. On the basis of twenty-five years selling millions of bottles which contain over 10,000 I.U. Vitamin A or 400 I.U. Vitamin D throughout the United States, we can reasonably conclude that our products are safe. Why then should we be prohibited from manufacturing and selling such products and why should we be forced to incur the disruption and expenditure required by the Vitamin A and D regulations which would be effective October 1, 1973?

I respectfully request that this Court grant plaintiff's motion herein for a preliminary injunction to preserve the status quo and prevent the irreparable injury we, as well as others in the industry, would suffer pending the presentation and consideration of plaintiffs' evidence which will demonstrate that the restrictions being imposed are medically and scientifically unreasonable and unsound.

PHILIP POLLACK

Sworn to before me this
13th day of August, 1973.

ROSE E. FOOSE
NOTARY PUBLIC OF NEW JERSEY
MY COMMISSION EXPIRES APR. 3, 1978

AFFIDAVIT OF HAROLD ROSENBERG
(Filed August 15, 1973)

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

THE NATIONAL NUTRITIONAL FOODS ASSOCIATION and SOLGAR CO., INC.,

Plaintiffs,

-against-

CASPER W. WEINBERGER, Secretary of Health, Education and Welfare, and ALEXANDER M. SCHMIDT, Commissioner of Food and Drugs,

Defendants.

Index No. 73 Civ. 3448

AFFIDAVIT

STATE OF NEW YORK)
) SS.:
COUNTY OF NEW YORK)

HAROLD ROSENBERG, D.O., being duly sworn, deposes and says:

I am an osteopathic physician licensed to practice medicine in the State of New York, and am a member of the New York State and New York City Osteopathic Societies.

I am immediate past president of the International Academy of Preventive Medicine. The members of the Academy include physicians, dentists and Ph.D's in the fields of medicine and science, and its members include such leaders in science and nutrition as Dr. Linus Pauling and Dr. Roger Williams. I am also a lifetime member of the New York Academy of Science and a staff member of the Leroy Hospital.

I am a graduate of Drake University where I received my B.A. in biological sciences. In 1951 I graduated the

Philadelphia College of Osteopathic Medicine and thereafter served my internship at the Swedish Hospital in Brooklyn, New York.

Preventive medicine and nutrition have been an intregal part of my work for over twenty years in private practice. In this time I have frequently had occasion to recommend to patients a substantial increase in their daily intake of vitamins and minerals. This includes the intake of levels of Vitamins A and D far beyond the 10,000 I.U. and 400 I.U. which the Food and Drug Administration seeks to fix as the maximum level available on a non-prescription basis. In all my years I have yet to encounter a single case of vitamin toxicity or symptomology of hypervitaminosis, be it Vitamin A or D or any other vitamin, among patients who have taken vitamins at levels far above the limitations which the FDA seeks to establish. Yet after October 1, 1973 I am told that any patient to whom I recommend Vitamin A at a level above 10,000 I.U. or Vitamin D at a level above 400 I.U. (even if it were just one I.U. more) will need a prescription which will have to be filled by a pharmacist.

The medical and scientific literature does not support such a general regulatory restriction on the availability of Vitamins A and D. These substances are essentially food substances. They are not dangerous per se. They are an essential part of human nutrition and differ from alien substances used for medication. Those studies on animals and man which report signs of Vitamin A or D toxicity, frequently deal with animals, infants and young children rather than adults. Even more frequently, and especially with adults, they involve levels

of hundreds of thousands and even millions of International Units of Vitamin A or D over extended periods of months or years before any signs of toxicity are noted.

It is my opinion, shared by many of my colleagues, that the FDA regulations requiring a prescription for any level of Vitamin A or D in excess of 10,000 I.U. or 400 I.U. is unreasonable and unnecessary and totally out of line with the tremendously high levels at which any signs of toxicity have been reported. If these low levels which FDA seeks to fix to non-prescription availability were sound, then innumerable food items, such as liver, sweet potatoes, and others would have to be limited to prescription use. It seems incredible that such food substances be limited to sale by prescription when we have many "over-the-counter" drug items, such as aspirin, which have well-documented histories of danger and abuse, available every day without prescription. I do not suggest that such drugs must necessarily be put on a prescription only limitation, but I do believe that such a limitation for more than 10,000 I.U. of Vitamin A or 400 I.U. of Vitamin D is most inappropriate and unjustifiable.

HAROLD ROSENBERG

Sworn to before me this

11th day of August, 1973.

SALOME LAUFER
NOTARY PUBLIC, State of New York
No. 31-4[illegible]
Qualified in [illegible] County

UNITED STATES DISTRICT COURT (Filed August 15, 1973)
SOUTHERN DISTRICT OF NEW YORK

THE NATIONAL NUTRITIONAL FOODS ASSOCIATION and SOLGAR CO., INC.,

Plaintiffs,

-against-

CASPER W. WEINBERGER, Secretary of Health, Education and Welfare, and ALEXANDER M. SCHMIDT, Commissioner of Food and Drugs,

Defendants.

Index No. 73 Civ. 3448

AFFIDAVIT

STATE OF NEW YORK)
) SS.:
COUNTY OF NEW YORK)

CARLTON FREDERICKS, being duly sworn, deposes and says:

I am a nutritionist and nutrition educator. I received my Ph.D. in Public Health Education from New York University. I have lectured, taught and studied in the field of nutrition since 1937. For many years I had a nationally syndicated radio program on nutrition and I still do many broadcasts in this field.

I have taught nutrition in the Continuing Education Divisions of Brooklyn College, City College and Rockland Community College, and was an adjunct professor in the Continuing Education Division of the New York Institute of Technology. At New York University I taught a course in applied nutrition for health supervisors and I was a member of the post-graduate faculty in nutrition of the Tenth District Dental Society of

New York. I also was an associate professor of nutrition and am presently a visiting professor of nutrition at Fairleigh Dickinson University.

I am a Fellow of the International Academy of Preventive Medicine and a Founding Fellow of the International Academy of Applied Nutrition. I have also been a member of the British Royal Health Society and am listed in several biographical indices including Who's Who in the East, Leaders in American Education, and others.

For many years I have been a staff and consulting nutritionist for various institutions, food and pharmaceutical companies. I am a nutrition consultant to physicians, dentists, osteopaths, psychiatrists, and other specialists. I am the author of various books and publications in the field of nutrition and one of my books, compiled in part from the subject matter of my radio broadcasts, was transcribed into Braille by the Library of Congress.

I am an avid reader of and keep current with the medical and scientific literature in the field of nutrition and keep in constant touch with the professional research in this field.

I am familiar with the bibliography cited by the Food and Drug Administration in connection with the regulation which would put Vitamin A and Vitamin D on prescription at levels above 10,000 I.U. for Vitamin A and 400 I.U. for Vitamin D. That bibliography rests heavily on observations of the effects of massive doses often administered by doctors, of these factors on animals and human beings. It omits citation of papers reporting use of equally large doses of Vitamins A and D, not only without evidence of toxicity, but with therapeutic benefit.

Thus, when Whipple received medical acclaim for his discovery that raw liver halted the progress of pernicious anemia, the medical literature reported no harm whatsoever in his patients, though their intake of liver three times daily was supplying them with at least 250,000 units of Vitamin A daily, for long periods of time. Dermatologists treating icthyosis (fishscale skin) with massive doses of Vitamin A over long periods of time, have reported no evidence of toxicity in children or adults. Individuals subject to repetitive attacks of kidney stone have been dosed with Vitamin A in massive amounts for long periods, with no evidence of toxicity. Jolliffe reported on the administration of Vitamin A in acne, with doses of 50,000 units daily and more, over extended periods of time; again, without observation of any toxic effects. Lobell administered large doses of Vitamin A, both by mouth and by intramuscular injection, in the treatment of otosclerosis, with therapeutic benefits unmarked by evidence of toxicity. Crampton prescribed 250,000 units of Vitamin A daily, both to abort colds and to reduce the severity of upper respiratory infections without report of any toxic effect.

Similarly with respect to Vitamin D Knapp has reported on the use of massive doses of Vitamin D in the treatment of myopia. An experience of more than 30 years with this therapy includes no observation of any case of Vitamin D toxicity. Massive doses of Vitamin D were reported in the 1930's to be therapeutically useful in the management of arthritis. Products then available had minimum potencies of Vitamin D, 50,000 units per capsule, and doses of 100,000 units and more, daily, were employed without toxic reactions to these dosages. While the FDA has cited cases of infants with an idiosyncrasy of metabolism

which renders them susceptible to toxic effects from Vitamin D at very low doses, it omits the evidence that there is a group of infants whose requirement for Vitamin D is raised to 100,000 units daily. Supplementation to offset this metabolic error must be in massive dosage, or florid rickets will develop. As much as the individual metabolic differences of the latter group should not be used to justify a ceiling of 100000 units of Vitamin D in consumer supplements for daily use, so should the metabolic aberration of the first group not be used to justify restrictions on the availability of genuinely protective amounts of Vitamin D for the average infant, child, and adult. Indeed, osteoporosis in the housebound geriatric population has recently been cited as grounds for more generous use of Vitamin D supplements for the aged who are denied exposure to sunshine.

The most innocuous substance can exhibit toxicity at some level of intake.

Massive doses of everyday foods and condiments would from some subjects prove toxic. Salt, substituted for sugar in infant formulae, has killed numerous babies. Nutmeg in modest dosage has caused hallucination in human beings. Overdoses of milk have been reported to cause calcification of the soft tissues in at least one human being. Large amounts of polyunsaturated fat, administered intravenously to an infant, have resulted in death. A puzzling sickness of an English patient was traced to overdoses of Worcestershire sauce, a condiment used without harm for many decades, by millions of consumers.

If the FDA definition of unsafe dosage of Vitamin A has merit, innumerable common food items consumed by the public should be put on a prescription-only basis. Carrot juice has been reported in large doses to cause carotemia - yellowing of the skin; but its content of Vitamin A, nearly 20,000 units per 8-ounce glass, has been innocuous, despite consumption of the juice, fresh squeezed or canned, by millions of Americans. Those who are fond of carrots, cooked or raw, may easily exceed FDA postulated toxic levels of Vitamin A intake. A modest portion of liver, eaten with spinach and a sweet potato, may yield nearly 80,000 units of Vitamin A.

It should also be noted that rather than there being a "danger" of excess intake of vitamins, the converse is the case. The Schaeffer study introduced at the FDA vitamin hearings from 1968 to 1970, demonstrated the existence of varied population groups whose dietary intakes were below those of the Recommended Dietary Allowance including Vitamin A for which the RDA is only 5,000 I.U. Older people who do not eat the "right" foods and who utilize the foods they do eat less efficiently, need more, not less, supplementation. Medically suggested diets based on the concept that animal fats and cholesterol are responsible for cardiovascular disease avoid the use of whole milk, even for infants, and reduce the intake of butter, liver, organ meats, and fats from meats and other animal proteins. These are measures which do not augment, but decrease the intake of Vitamin A. Recent studies of the U.S.D.A. report a <u>drop</u> in Vitamin A intake in the last two decades.

Dr. Linus Pauling has estimated that the range of require-

ment for Vitamin A in human beings may go from 5,000 units daily to 25,000. It is evident that the F.D.A. proposal to limit Vitamin A potencies to 10,000 units heavily penalizes those whose metabolism does not coincide with that of the mythical "standard reference American".

Vitamin A supplementation is not an invention of the modern vitamin industry. The history of the use of supplements of Vitamins A and D, beginning with codliver oil, is at least a century old. It is not a history of episodes of toxic reactions, but one of benefit to the public. What happens to animals given massive doses of these vitamins, or what has happened to human beings astronomically overdosed with these factors should not be permitted to deprive the great majority of Americans of Vitamin A and D supplements of effective potency. The non-prescription limits of 10,000 I.U. of Vitamin A and 400 I.U. of Vitamin D which the F.D.A. now proposes to fix by regulation are unreasonable and not supported by scientific fact.

s/
CARLTON FREDERICKS

Sworn to before me this
4th day of August, 1973.

ROBERT ULLMAN
Notary Public, State of New York
No. 30-4603770
Qualified in Nassau County
Commission Expires March 30, 1975

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

THE NATIONAL NUTRITIONAL FOODS ASSOCIATION and SOLGAR CO., INC.,

Plaintiffs,

-against-

CASPER W. WEINBERGER, Secretary of Health, Education and Welfare, and ALEXANDER M. SCHMIDT, Commissioner of Food and Drugs,

Defendants.

Index No. 73 Civ. 3448

AFFIDAVIT

STATE OF NEW YORK)
) SS.:
COUNTY OF NEW YORK)

ROBERT ULLMAN, being duly sworn, deposes and says:

I am a member of the firm of Rees & Ullman, attorneys for plaintiffs in this action, and submit this affidavit in connection with plaintiffs' motion for a preliminary injunction herein.

The instant motion by plaintiffs seeks an order, pending a determination of the issues raised by plaintiffs' complaint for a declaratory judgment and permanent injunction, staying enforcement by the Food and Drug Administration (FDA) of new regulations which would require the sale of Vitamin A at levels above 10,000 International Units (I.U.) and Vitamin D at levels above 400 I.U. to be on a prescription only basis.

Annexed hereto as Exhibit "A" is a copy of pages 20723-20725 of the Federal Register of Thursday, August 2, 1973

(Vol. 38, No. 148) wherein the new regulations are set forth. These regulations would become a part of the Code of Federal Regulations (21 CFR §§3.94 and 3.95).

Annexed hereto as Exhibit "B" is the Federal Register publication of December 14, 1972 wherein the FDA announced for the first time its proposal to impose the aforementioned prescription requirements on Vitamins A and D. This announcement invited written comments by interested persons (at page 26620) and in the first page (pg. 26618) states that a list of pertinent articles regarding these vitamins is available to the public at the office of the Hearing Clerk in Rockville, Maryland. Plaintiff National Nutritional Foods Association (NNFA) filed its comments and objections to the FDA proposal including an analysis of the articles referred to in the December 14 announcement. A copy of those comments, objections and analysis is annexed hereto as Exhibit "C". Almost all of these articles involve the use of Vitamin A and D at levels far above and beyond the prescription levels in the new FDA regulations.

Annexed hereto as Exhibit "D" is a copy of pages 21-28 of the 1968 Recommended Dietary Allowances (RDA) publication of the Food and Nutrition Board of the National Research Council, National Academy of Sciences. Considering Vitamin A, for which the RDA is set at 5,000 I.U., the Food and Nutrition Board states at page 23:

> "If large doses of vitamin A (20 to 30 times RDA) or of carotene are ingested for long periods of time, manifestations of toxicity develop."

Considering Vitamin D, the Food and Nutrition Board states at pages 25 and 26:

> "[E]xcessive amounts of vitamin D (of the order of 1,000 to 3,000 iu/kg/day) are potentially dangerous to children and adults and may lead to hypercalcemia and attendant complications....There is no evidence that intakes of the order of 2,000 to 3,000 iu/day produce hypercalcemia beyond infancy."

Annexed hereto as Exhibit "E" is a statement in the Congressional Record of June 7, 1973 (Pg. E3847-3849) by Dr. Linus Pauling, two-time Nobel Prize winner, criticizing the prescription limitations which FDA seeks to impose upon the use of Vitamins A and D. Dr. Pauling states that the optimum daily intake of Vitamin A for many people is 25,000 I.U. and that there is no convincing scientific evidence to support the new regulation. He also observes that FDA's limitations could be extended to ordinary portions of common foods containing amounts of Vitamin A far above 10,000 I.U. Dr. Pauling is a Professor of Chemistry at Stanford University and was Chairman of the Division of Chemistry and Chemical Engineering at the California Institute of Technology. His credentials are set forth at length at page E3848 of the Congressional Record.

Annexed hereto as Exhibit "F" is a statement dated August 8, 1973 of Dr. E. Cheraskin, M.D., D.M.D. Dr. Cheraskin is an Assistant Professor in the Department of Medicine at the University of Alabama Medical Center and Professor and Chairman of the Department of Oral Medicine. His work in clinical nutrition, and appointment, memberships, publications and honors are set forth in the curriculum vitae annexed to his statement. Considering the FDA's new regulations on Vitamins A and D, Dr. Cheraskin states:

"On the basis of my personal experience and my knowledge of the literature, I find it difficult to justify the recent pronouncements by the Food and Drug Administration regarding the dosages of vitamins A and D acceptable for over the counter use."

Annexed hereto as Exhibit "G" is a statement dated August 7, 1972 of Harvey Ross, M.D., Los Angeles, California, expressing his disagreement with the FDA restrictions on Vitamins A and D based on his experience and medical knowledge. Dr. Ross was Vice President of the Gracie Square Hospital Medical Board in New York and is a member of the Board of Governors of the International College of Applied Nutrition. His curriculum vitae is annexed to his statement.

Annexed hereto as Exhibit "H" is a statement dated August 7, 1973 from Dr. J. P. Hutchins, M.D., President of the International College of Applied Nutrition, who states that in his 20 years of medical practice he has not encountered any case of toxic effects among his patients who have taken Vitamin A in excess of 10,000 I.U. per dosage and Vitamin D in excess of 400 I.U. per dosage daily. Dr. Hutchins further states that the prescription limitations fixed by the FDA for Vitamins A and D are unreasonable and without any valid purpose.

The National Clearing House for Poison Control Centers, United States Department of Health, Education and Welfare, Public Health Service, Food and Drug Administration has issued a Bulletin dated April-June, 1972 on the subject matter of "Vitamin Ingestions." Considering the question of Vitamin A intoxication or hypervitaminosis A, the Bulletin states, at page 4 thereof, "Hypervitaminosis A has, with one exception, been associated with intake of

more than 100,000 I.U. a day." Similarly, with respect to Vitamin D, this Bulletin states, at pages 4 and 5, "from an acute single ingestion standpoint, Vitamin D is non-toxic" and that "ingestion of Vitamin D in doses of 100,000 units or more daily in adults or 4,000 units or more daily in children has resulted in hypervitaminosis D." A copy of the Bulletin is annexed hereto as Exhibit "I"

Between 1968 and 1970, the FDA conducted public hearings with respect to regulations dealing with the label statements for dietary supplements of vitamins and minerals and the creation of a standard of identity for vitamin-mineral supplements. The transcript of these two-year public hearings alone consumed over 32,000 pages. The regulations covered by those hearings were actually first proposed in 1962 and were not finalized until August 2, 1973. The final order promulgating these regulations is now the subject of a petition for review before the Court of Appeals. At no time from 1962 through the public hearings, which ended in 1970, and up to December 14, 1972, was any suggestion ever made that the non-prescription use of Vitamins A and D be limited to levels not to exceed 10,000 U.U. and 400 I.U. respectively. Although the public hearings did not deal with any such question of establishing prescription limitations, FDA's own witnesses at these hearings gave testimony as to the exceedingly high levels at which there have been reports of toxic symptoms in the use of Vitamins A and D.

Annexed as Exhibit "J" is a copy of page 2361 of the aforesaid public hearings wherein Dr. Arthur Grollman, M.D. agreed with the statement in his own text that there was little,

if any, evidence of Vitamin D toxicity and that the only cases of Vitamin A toxicity with which he was familiar involved doses of 100,000 I.U. per day over an extended period of time. The relevant pages of Dr. Grollman's text were also received in evidence and copies thereof are attached to the transcript page of his testimony. Dr. Grollman testified as a pharmacologist and as Professor of Experimental Medicine at the University of Texas, Southwestern Medical School.

Annexed hereto as Exhibit "K" is a copy of pages 14,572 and 14,573 of the transcript of the aforesaid hearings wherein FDA witness, Dr. Victor Herbert, M.D., testified that Vitamin A toxicity could occur with amounts in excess of 100,000 units per day. Dr. Herbert testified as an expert in nutrition and as a Professor of Medicine at the Mt. Sinai School of Medicine, New York, New York.

Annexed hereto as Exhibit "L" is a copy of page 23,230 wherein Dr. Harold E. Harrison, M.D. testified that the level at which manifestations of Vitamin A toxicity occurs would be in the neighborhood of 100,000 I.U. per day over several months. Dr. Harrison testified for the FDA in his capacity as Pediatrician in Chief of the Department of Pediatrics, Baltimore City Hospital and Professor of Pediatrics at Johns Hopkins University School of Medicine. He was also a committee member of the Recommended Daily Allowances Committee of the Food and Nutrition Board.

Annexed hereto as Exhibit "M" is a copy of pages 14,766 to 14,770 of the aforesaid transcript wherein FDA witness Professor Olaf Mickelsen, Ph.D. testified that toxicity with

respect to Vitamins A and D may occur at levels far higher than the RDA's of Vitamins A and D, such as 50,000 to 500,000 I.U. of Vitamin A in children and 150,000 I.U. of Vitamin D per day in adults. Dr. Mickelsen testified as a Professor of Bio-Chemistry and Nutrition at Michigan State University; he was also Secretary of the American Institute of Nutrition and a Member of the Editorial Board of the Journal of Nutrition.

Annexed hereto as Exhibit "N" is a listing of everyday common food items extracted from the United States Department of Agriculture Handbook No. 8. This list sets forth innumerable food items, any one of which contain between 5,100 and 100,000 I.U. of Vitamin A in a single 100 gram (approximately 3-1/2 oz.) edible portion. The entire Handbook No. 8 will be submitted to the Court with the instant motion.

Further affidavits setting forth medical and scientific disagreement with the FDA restrictions on non-prescription use of Vitamins A and D are being submitted with this motion. On the basis of the documents submitted herewith, including the affidavits of irreparable injury which will be caused by these regulations if theyare not stayed pending a final determination of the issues, and the arguments set forth in plaintiffs' accompanying memorandum, it is respectfully requested that plaintiffs' motion for a preliminary injunction be granted.

ROBERT ULLMAN

Sworn to before me this

day of August, 1973.

chase, the words prescribed by this paragraph shall immediately and conspicuously precede or follow such name, except:

(i) Where the characterizing flavor and a trademark or brand are presented together, other written, printed, or graphic matter that is a part of or is associated with the trademark or brand may intervene if the required words are in such relationship with the trademark or brand as to be clearly related to the characterizing flavor; and

(ii) If the finished product contains more than one flavor subject to the requirements of this paragraph, the statements required by this paragraph need appear only once in each statement of characterizing flavors present in such food, e.g., "artificially flavored vanilla and strawberry."

PART 3—STATEMENTS OF GENERAL POLICY OR INTERPRETATION

§ 3.10 [Revoked]

2. The provisions of § 3.10 are hereby revoked.

§ 3.23(b) [Revoked]

3. The provisions of § 3.23(b) are hereby revoked.

§ 3.201 [Revoked]

4. The provisions of § 3.201 are hereby revoked.

Effective date. Labeling may be changed to comply with this regulation beginning August 2, 1973. All labeling ordered on or after December 31, 1973, and all labeling used for products shipped in interstate commerce on or after December 31, 1974, shall comply with this regulation; provided, that the label of a flavor need not conform to paragraph (g)(2) of this regulation prior to December 31, 1974, if it bears a statement certifying that the ingredients are listed as being generally recognized as safe on a reliable published industry association list.

(Secs. 403, 701(a), 52 Stat. 1047, 1055; 21 U.S.C. 343, 371(a))

Dated: July 25, 1973.

A. M. SCHMIDT,
Commissioner of Food and Drugs.

[FR Doc.73-15700 Filed 8-1-73;8:45 am]

PART 3—STATEMENTS OF GENERAL POLICY OR INTERPRETATION

Status of Vitamin A and Vitamin D

In the FEDERAL REGISTER of December 14, 1972 (37 FR 26618) the Commissioner of Food and Drugs proposed that preparations containing vitamin A in excess of 10,000 international units (IU) per dosage unit and preparations containing vitamin D in excess of 400 IU per dosage unit shall be dispensed on prescription. A correction, which did not alter the intent of the proposal, was published in the FEDERAL REGISTER of January 4, 1973 (38 FR 799). Sixty days were allowed for comment.

Approximately 1,000 signatures on petitions received in response to the proposal were received from a small segment of the public, including individual consumers, physicians, nurses, pharmacists, dietitians, home economists, nutritionists, nine pharmaceutical manufacturers, a number of vitamin preparation distributors, and health food store operators. Comments from the medical profession were presented by the American Academy of Pediatrics and the American Medical Association. Organized consumer groups that responded were the National Health Federation, Oregon Student Public Interest Research Group, Committee Against Health Fraud, Inc., Committee for the Cessation of "Fortification" of Food Products with Calciferol Hormones, Virginia Citizens Consumer Council, Inc., Consumers Cooperative of Berkeley, Inc. Comments were also submitted by the Wisconsin Alumni Research Foundation, The Ann Arbor Dietetic Association, the American Dietetic Association, and five trade associations: The Pharmaceutical Manufacturers Association, East Coast Health Food Corporation, the National Food, Drug and Cosmetic Association of Manufacturers and Distributors, Inc., the National Nutritional Foods Association and the National Association of Pharmaceutical Manufacturers.

GENERAL COMMENTS

The proposal was controversial and generated widely ranging comments regarding broad issues raised by the use of vitamins in foods and drugs. Many of these comments are not appropriate for consideration of the more limited issues raised in the proposed regulation regarding vitamin A and vitamin D. With respect to the broad issues of vitamin and mineral use the Commissioner notes that several regulations including comprehensive discussion of these issues have been published in the FEDERAL REGISTERS of January 19 and March 14, 1973 (38 FR 2124, 6950) and elsewhere in this issue of the FEDERAL REGISTER.

The majority of responses from individual consumers were opposed to the proposal. In reviewing such comments, the Commissioner is concerned that the public is not fully aware of the provisions and medical basis of the proposal. For example, the tenor of many comments was that vitamin A and vitamin D would be available only on prescription. Form letters and several petitions, which were submitted with a number of signatures, contained key statements, presumably the basis on which the signatures were obtained, that bear very little, if any, resemblance to the actual provisions of the proposal. It is clear that the majority of individual consumers responding had been improperly or inadequately informed.

The comments fall into three general categories:

(1) Those who agree that the action proposed by the Food and Drug Administration is necessary and that the prescription levels proposed for vitamin A and vitamin D are suitable. Those who agreed included the American Academy of Pediatrics, the American Medical Association, five consumer groups, numerous physicians, dietitians, nutritionists, home economists and other professionals in the scientific and health care community, and a few individual consumers.

(2) Those who agree that such vitamins can be toxic, but only at levels higher than those levels proposed by the Food and Drug Administration. The majority of the drug manufacturers and trade associations, and some consumers, made responses that were in this category.

(3) Those who disagree with the proposal entirely, stating that such vitamins are foods and that individuals should have the right to ingest any amount desired. The comments from most individual consumers, operators of health food establishments and a consumer group, were in this category.

SPECIFIC COMMENTS

1. A number of comments contended that "natural" vitamins (including vitamin A and vitamin D) and minerals are foods rather than drugs and should not be treated as drugs. Some viewed "natural" vitamins as safe whereas synthesized vitamins may be (or are) toxic.

The question regarding whether a vitamin is a food or drug generated considerable discussion. The tentative and final orders promulgating §§ 80.1, 125.1, and 125.3 (21 CFR 80.1, 125.1 and 125.3), published in the January 19, 1973 FEDERAL REGISTER (38 FR 2143, 2152) and elsewhere in this issue of the FEDERAL REGISTER discuss this matter in detail. The Commissioner concludes, on the basis of all the available evidence, that vitamins between the upper and lower limits as specified in § 80.1 are adequate for all known nutritional needs for normal individuals and that nutrients at these levels are dietary supplements which are foods for special dietary use. No evidence was submitted in the comments to establish a food or nutritional use of vitamin A or vitamin D at higher levels, except for a limited number of persons with poor vitamin D absorption who need up to 1000 IU of this vitamin for nutritional purposes under medical supervision. With that one exception, which is recognized in the revised regulation, intake of vitamins at levels exceeding the upper limits as specified in § 80.1 are therefore appropriate only for therapeutic purposes and thus are properly classed as drugs.

This position is entirely consistent with the Food and Drug Administration's long-standing interpretation and application of the act. See, e.g., Kordel v. United States, 335 U.S. 345 (1948), in which the Supreme Court upheld the conviction of an individual for marketing "health food products" consisting of "various vitamins, minerals, and herbs" on the ground that they were misbranded drugs. See also United States v. 3 Cartons * * * "No. 26 Formula GM etc.," 132 F. Supp. 569 (S.D. Calif. 1952).

Alleged differences in vitamins based on their source is also discussed in the

ıtative and final orders promulgating 30.1 and 125.1–125.3. There is no scie- ific evidence to suggest that there is lifference in the metabolic actions or ic effects of synthetically produced mins as compared with those from tural sources.

. Several manufacturers and trade ociations objected to the proposal on ground that the proper classification OTC drug levels of vitamins would made in the near future by the ap- priate OTC drug advisory review el and that levels established now the Food and Drug Administration uld only be on interim measure. se comments expressed the opinion t deferring action on this proposal uld not result in any significant haz- to the public health.

n the preamble of the proposal the nmissioner stated his reasons for arating vitamin A and vitamin D m the other vitamins at this time and ablishing levels above which these mins are limited to prescription dis- ution. The continuing information ilable to the Commissioner regarding toxicity of vitamin A and vitamin D l the continuing reports of promotion large amounts of these vitamins for ariety of purposes makes this action essary at this time in the public in- est.

. A number of comments from indi- ual consumers and those representing vitamin industry agreed that vitamin nd vitamin D are toxic in amounts excess of known requirements, but ed that such levels are much higher n the limitations proposed. Some nments offered a level of 25,000 IU of amin A and 1,000 IU of Vitamin D as viding a sufficient safety margin for wn toxicity. Other comments con- ded that the proposed levels were table for children, but higher levels uld be more appropriate for adults. A mber of comments felt the proposed els were arbitrary and without scien- c merit or support. Several of the nments had made a review and pro- ed their own analysis of the bibliogra- y prepared by the Food and Drug Ad- nistration at the time the proposal published in the FEDERAL REGIS- R. Generally, these comments stated t toxicity below 50,000 IU daily for amin A was rare and that vitamin D icity reports would not support the min D level proposed.

everal other comments recommended er levels than those proposed. A nment from a physician at a uni- sity School of Medicine, Department Biochemistry, supported the proposal, stated that 5,000 IU for vitamin A uld be a more judicious level. Another nment from the Department of Chem- Pathology, the United Liverpool Hos- ls, Liverpool, England, included a erence to a paper written by the re- ndent regarding self-medication with ltivitamin preparations and recom- nded that 100 IU of vitamin D per age unit be the limit for non-pre- iption marketing.

The Commissioner has carefully re- wed the comments and analysis re- garding the recommendation for establishing the proposed vita- min A and vitamin D limits and finds that such comments do not sufficiently support a revision of the proposed limits. No evidence refuted the toxicity findings on which the proposal was based, and further reports of toxicity continue to accumulate. Based on consultation with the most knowledgeable experts available, the Commissioner finds that the scientific consensus is that the proposed limits are appropriate at this time.

The Commissioner of Food and Drugs will soon publish in the FEDERAL REGISTER a request for submission of all data and information relevant to the safety and effectiveness of vitamins and minerals for OTC drug use, pursuant to the procedures established in 21 CFR 130.301, published in the FEDERAL REGISTER on May 11, 1972 (37 FR 9464). The members of the OTC drug review panel for vitamin-mineral drugs are presently being selected. This panel will have full authority to review and re-evaluate the proper dividing line between OTC and prescription levels of vitamin A and vitamin D, and to recommend to the Commissioner any changes in the regulations promulgated by this order, in its report. Thus, the levels of vitamin A and vitamin D for prescription use in this regulation are established on an interim basis only. These regulations will be revoked upon promulgation of a final OTC drug monograph for vitamin-mineral drugs incorporating final prescription levels for these two vitamins.

4. A number of comments, particularly those from individual consumers, state that it is not logical to require a prescription for dosage levels of vitamins that may be lower than the vitamin content of an average serving of certain foods. A few comments expressed concern that normal diets with or without appropriate vitamin supplementation may lead to toxic conditions.

The Commissioner recognizes that many common foods contain a variety of vitamins and minerals in widely ranging amounts, and that some common foods contain vitamin A in excess of 10,000 IU per serving. It is also recognized, however, that these foods particularly rich in vitamin A are rarely consumed daily in sufficient quantity over the long periods of time required to lead to toxic manifestations. The concern of the Food and Drug Administration is the availability of vitamin A and vitamin D in large dosage units in medicinal forms, i.e. capsules and tablets, particularly in view of the multiplicity of other sources of this vitamin in the daily diet. The convenience of ingestion in this form on a routine basis encourages excessive intake of these vitamins far beyond the average amounts ingested in normal diets of conventional food over extended periods of time. Adequate amounts of vitamin A and vitamin D will continue to be available as dietary supplements and are not being removed from the market place. The margins of safety provided in the levels established by this proposal were developed to take into account the wide ranges of vitamin of vitamin A and [illegible] that are usually implicated in toxic conditions.

5. Comment was received that consumers would be able to ingest as many dosage units as they desired and therefore the proposed limits would have no effect. The Commissioner cannot agree with this concept. Today's consumers are increasingly knowledgeable and are concerned about the health and safety of themselves and their family. The Commissioner believes that most consumers will carefully consider the advisability of taking dosage units in excess of suitable recommended daily dosages. Conscientious consumers will have a basis upon which to make a judgment as to their intake of these vitamins. The fact that a small number of consumers will abuse their health by excessive intakes of drugs, regardless of regulatory and other approaches to curtail such abuse, is no reason to forego a reasonable regulation that will afford appropriate public health protection for the vast majority of the public.

6. The Committee on Nutrition, American Academy of Pediatrics, and several other respondents commented on the special needs for vitamin D in foods for special dietary use in specific medical conditions. Foods designed to provide sound nutrition to individuals with poor vitamin D absorption require higher than normal levels of vitamin D. Such individuals may require dietary intakes up to 1000 IU as part of their overall dietary management.

The Commissioner recognizes that foods represented solely for use under medical supervision to meet nutritional requirements in specific medical conditions have a place in medical care of a select group of individuals who have diagnosed conditions that will benefit from the use of complete foods containing up to 1000 IU of vitamin D. The marketing of such foods is permitted in compliance with § 125.1(h) being published elsewhere in this issue of the FEDERAL REGISTER. The regulation for vitamin D has been revised to allow this limited use of a higher amount of vitamin D without a prescription.

7. Comments received from the Council on Foods and Nutrition, American Medical Association, endorse the proposal and include reference to the possible relationship between excess vitamin D and hypercholesterolemia, in addition to the classic form of vitamin D toxicity. The Council also commented that the proposal fails to mention that there is no recommended dietary allowance for vitamin D for adults, since their needs are considered to be met by ordinary mixed diets and exposure to sunlight. The Council, along with other respondents, raised a question regarding a controlled "overage" to assure compliance with label declarations of the amounts present.

The Food and Drug Administration recognizes that there is no recommended dietary allowance for vitamin D in adults except during pregnancy and lactation and therefore considers vitamin D as an

optional component of dietary supplements of vitamins and minerals for adults and older children (21 CFR 80.1). The Commissioner notes that within good manufacturing practices reasonable overages are permissible in formulating drugs and these are recognized in the specification ranges used in determining whether or not a product meets its labeled potency.

8. In response to the proposal, the Wisconsin Alumni Research Foundation resubmitted comments directed to a proposal regarding vitamin D published in the FEDERAL REGISTER of August 28, 1965 (30 FR 11140). The previous proposal was more restrictive than the present one and contained several provisions not currently being considered. Of significance in the comment was concern by the Wisconsin Alumni Research Foundation that the requirements as proposed in 1965 would have the effect of decreasing the vitamin D intake by the general public to a level below their nutritional needs.

The Commissioner concludes that such a situation is clearly not possible as a result of the current proposal, which is directed only at the use of vitamin D as a drug. As a result of the vitamin D content of milk and other foods, and the availability of vitamin D in dietary supplements, the national food supply provides ample vitamin D.

9. Several manufacturers commented that the effective date of any final order with respect to vitamin A and vitamin D should be the same uniform effective date established for recent food labeling revisions. Such an effective date would permit interstate shipments of existing high potency products through December 31, 1974. Several comments also requested that those vitamin A and vitamin D preparations already in commercial channels be allowed continued marketing until existing supplies are exhausted.

Because of the known toxicity and continuing reports of toxic conditions resulting from large dosages over a period of time, the Commissioner concludes that protracted continuation of manufacture and marketing of preparations that do not meet the requirements of this order is not justified. However, a reasonable period of time to allow for orderly reformulation and relabeling, where necessary, is in the public interest to assure continued availability of vitamin A and vitamin D preparations. Therefore, this order shall become effective for products labeled beginning October 1, 1973. No recall of existing stocks is deemed necessary.

10. One comment from a manufacturer stated that the proposal conflicts with the limits for vitamin A established by the food labeling regulations published in the January 19, 1973 FEDERAL REGISTER (38 FR 2124). The Commissioner finds no conflict between this drug regulation and the food regulations. Those vitamin A preparations within the ranges specified in § 80.1 are considered foods and must be labeled as dietary supplements. Those preparations containing vitamin A in excess of the upper limit of these ranges, but less than the proposed prescription drug level, are OTC drugs. Those preparations containing in excess of 25,000 IU of vitamin A per dosage unit are prescription drugs.

11. Several comments requested that a public hearing be held to consider the issues and objections. A hearing on these matters is not mandatory under section 701(a) of the act. The Commissioner concludes that a hearing is inappropriate at this time and that any further delay in promulgation of these regulations is not in the public interest. A hearing on this issue will be available before both the advisory drug panel and the Commissioner under the OTC drug review procedures.

Having considered the comments received, the Commissioner concludes that the proposed regulations are in the public interest and should be adopted as set forth below.

Therefore, pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (secs. 502(a), (f), and (j), 503(b), 701(a), 52 Stat. 1050–1053, as amended, 1055; 21 U.S.C. 352(a), (f), and (j), 353(b), 371(a)) and under authority delegated to the Commissioner (21 CFR 2.120), Part 3 is amended by adding thereto the following new sections:

§ 3.94 Vitamin A preparations for oral use as drugs.

(a) Vitamin A is an essential nutrient for humans. It is widely recognized that large amounts of vitamin A can cause adverse effects, some of which are serious. The U.S. Recommended Daily Allowance (U.S. RDA) for vitamin A is 1500 International Units, (IU) for infants, 2500 IU for children under 4 years of age, 5000 IU for adults and children 4 or more years of age, and 8000 IU for pregnant or lactating women.

(b) In view of the toxicity of excessive consumption of vitamin A, the Food and Drug Administration finds that, in order to protect the public health, oral preparations containing vitamin A in excess of 10,000 IU per dosage unit or recommended daily intake are drugs subject to section 503(b)(1) of the Federal Food, Drug, and Cosmetic Act and shall be restricted to prescription sale. Such products will be regarded as misbranded if at any time prior to dispensing the following conditions are not met:

(1) The label bears the legend, "Caution: Federal law prohibits dispensing without a prescription"; and

(2) The labeling bears full disclosure information as required by § 1.106(b)(3)(i) of this chapter, and especially appropriate warnings regarding vitamin A toxicity.

(c) Preparations containing 10,000 or less IU of vitamin A per dosage unit will be regarded as misbranded if their recommended daily intake exceeds 10,000 IU.

§ 3.95 Vitamin D preparations for oral use as drugs.

(a) Vitamin D is an essential nutrient for humans. It is widely recognized that vitamin D, when ingested daily in large amounts, is toxic. The U.S. Recommended Daily Allowance (U.S. RDA) for vitamin D is 400 International Units (IU).

(b) In view of the toxicity of the excessive consumption of vitamin D, the Food and Drug Administration finds that, in order to protect the public health, oral preparations containing vitamin D in excess of 400 IU per dosage unit or recommended daily intake are drugs subject to section 503(b)(1) of the Federal Food, Drug, and Cosmetic Act and shall be restricted to prescription sale. Such products will be regarded as misbranded if at any time prior to dispensing the following conditions are not met:

(1) The label bears the legend, "Caution: Federal law prohibits dispensing without a prescription"; and

(2) The labeling bears full disclosure information as required by § 1.106(b)(3)(i) of this chapter, and especially appropriate warnings regarding vitamin D toxicity.

(c) Preparations containing 400 or less IU of vitamin D per dosage unit will be regarded as misbranded if their recommended daily intake exceeds 400 IU.

(d) Foods which are represented for use solely under medical supervision to meet nutritional requirements of persons with poor vitamin D absorption may contain vitamin D not in excess of 1000 IU per dosage unit or recommended daily intake.

Effective date. This order shall become effective on October 1, 1973 for products labeled on or after that date.

(Secs. 502(a), (f), and (j), 503(b), 701(a), 52 Stat. 1050–1052, as amended, 1055; 21 U.S.C. 352(a), (f), and (j), 353(b), 371(a))

Dated: July 25, 1973.

A. M. SCHMIDT,
Commissioner of Food and Drugs.

[FR Doc.73-15703 Filed 8-1-73;8:45 am]

PART 3—STATEMENTS OF GENERAL POLICY OR INTERPRETATION

SUBCHAPTER B—FOOD AND FOOD PRODUCTS

PART 121—FOOD ADDITIVES

Folic Acid, Potassium Iodide and Kelp

In the FEDERAL REGISTER of January 19, 1973, the Commissioner of Food and Drugs published tentative orders revising regulations for food for special dietary uses and establishing a definition and standard of identity for dietary supplements of vitamins and minerals (38 FR 2143, 2152). In the preamble to the tentative order revising the regulations for foods for special dietary uses, the Commissioner stated that other regulations governing the levels of the food additives folic acid and iodine would be revised at a later date to make them consistent with the levels of these nutrients permitted in foods for special dietary uses and in dietary supplements of vitamins and minerals (38 FR 2145).

No exceptions were received objecting to the provisions of the two tentative orders relating to the levels for folic acid and iodine. Elsewhere in this issue of the FEDERAL REGISTER the Commissioner is publishing a final order promulgating those new regulations with the levels for folic acid and iodine unchanged.

...yield times one-half the sum of the figure 1 and the national factor for the current year, or (2) the farm marketing quota for the immediately preceding marketing year times one-half factor for the current year. The farm marketing quota so computed for any farm for any year shall be increased by the number of pounds by which marketings from the farm during the immediately preceding year were less than the farm marketing quota (after adjustments): *Provided*, That any such increase shall not exceed the amount of the farm marketing quota (including leased pounds) for the immediately preceding marketing year prior to any increase for undermarketings or decrease for overmarketings. The farm marketing quota so computed for each farm for any year shall be reduced by the number of pounds by which marketing from the farm during the immediately preceding year exceeded the farm marketing quota (after adjustments): *Provided*, That if, on account of excess marketings in the preceding year, the farm marketing quota is reduced to zero pounds without reflecting the entire reduction required, the additional reduction required shall be made in subsequent marketing years.

Section 319(e) provides also, that the farm marketing quota for a new farm shall be the number of pounds determined by the county committee with approval of the State committee to be fair and reasonable for the farm on the basis of the past burley tobacco experience of the farm operator; the land, labor, and equipment available for the production of burley tobacco; crop rotation practices, and the soil and other physical factors affecting the production of burley tobacco: *Provided*, That the farm marketing quota for any such new farm shall not exceed 50 percent of the average of the farm marketing quotas for similar farms for which farm marketing quotas are otherwise established: *Provided further*, That the number of pounds allocated to all new farms shall not exceed that portion of the national reserve provided by the Secretary for establishing quotas for new farms.

Section 319(h) provides that effective with the marketing year beginning October 1, 1976, no marketing quota, other than a new farm marketing quota, shall be established for a farm on which no burley tobacco was planted or considered planted in any of the 5 years immediately preceding the year for which farm marketing quotas are being established.

Section 319(i) provides, in part, that if the Secretary, in his discretion, determines it is desirable to encourage additional marketings of any grades of burley tobacco during any marketing year to insure traditional market patterns to meet the normal demands of export and domestic markets, he may authorize the marketing of such grades without the payment of penalty or deduction from subsequent quotas to the extent of 5 percent of the farm marketing quota for the farm on which the tobacco was produced, and such marketings shall be eligible for price support.

The Act (7 U.S.C. 1301(b)) defines the "reserve supply level" as the normal supply plus 5 percent thereof. "Normal supply" is defined as a normal year's domestic consumption and exports, plus 175 percent of a normal year's domestic consumption and 65 percent of a normal year's exports. A "normal year's domestic consumption" is defined as the yearly average quantity produced in the United States and consumed in the United States during the 10 marketing years immediately preceding the marketing year in which such consumption is determined, adjusted for current trends in such consumption. A "normal year's exports" is defined as the yearly average quantity produced in the United States which was exported from the United States during the 10 marketing years immediately preceding the marketing year in which such exports are determined, adjusted for current trends in such exports.

The subjects and issues involved in the proposed determinations with respect to burley tobacco for the 1973–74 marketing year are:

1. The amount of the reserve supply level.
2. The amount of the national marketing quota.
3. The amount of the national reserve.
4. The national factor.
5. Whether the Secretary should implement the provision in section 319(i) to encourage additional marketings of any grades to insure traditional market patterns.

Consideration will be given to data, views, and recommendations pertaining to the proposed determinations, rules and regulations covered by this notice which are submitted in writing to the Director, Tobacco Division, Agricultural Stabilization and Conservation Service, U.S. Department of Agriculture, Washington, D.C. 20250. All written submissions made pursuant to this notice will be made available for public inspection from 8:15 a.m. to 4:45 p.m., Monday through Friday, in Room 3741, South Building, 14th and Independence Avenue, SW., Washington, D.C. All submissions must, in order to be sure of consideration, be postmarked not later than 30 days from the date of publication of this notice in the FEDERAL REGISTER.

Signed at Washington, D.C. on December 7, 1972.

GLENN A. WEIR,
Acting Administrator, Agricultural Stabilization and Conservation Service.

[FR Doc.72-21502 Filed 12-13-72;8:49 am]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration

[21 CFR Part 3]

VITAMIN A AND VITAMIN D

Proposed Statement of Policy

Large doses of vitamin A and/or vitamin D ingested over long periods of time can cause adverse effects, some of which are serious. Vitamins A and D are fat-soluble and excess quantities accumulate in fatty tissue. The acute and chronic toxicity of these vitamins is documented extensively in the medical literature. Vitamin A is available over the counter in dosage levels up to 10 times the recommended daily dietary allowance (RDA) of the Food and Nutrition Board, National Academy of Sciences-National Research Council (FNB-NRC), and vitamin D is available up to 60 times the RDA. The availability without prescription of these vitamins in high dosage levels contributes significantly to their misuse and the occurrence of serious adverse effects.

In view of the toxicity of excessive quantities of these vitamins, it is of concern to the Food and Drug Administration and medical authorities that there is widespread promotion to the laity of excessive quantities of these vitamins for prophylaxis and treatment of a variety of diseases and disorders. In its "Newsletter" of June 1, 1972 (Vol. 23, No. 9), the American Academy of Pediatrics (AAP) comments on the critical dangers of use of high doses of vitamin A that have been recommended in the lay press, on radio, and on television. For example, the layman is being advised that he would profit from taking 25,000 international units (IU) of vitamin A with 2,500 IU of vitamin D, or twice these amounts, daily.

The AAP Committee on Drugs and on Nutrition published a joint committee statement entitled "The Use and Abuse of Vitamin A" in the journal "Pediatrics," Volume 48, Number 4, October 1971, warning physicians regarding vitamin A toxicity. This article states "Despite awareness of the potential dangers of vitamin A toxicity, the incidence of hypervitaminosis A appears to be increasing. Hypervitaminosis A may result through easy availability of high potency vitamin preparations without prescription and by the overzealous parents who frequently administers vitamins under the popular premise, that, if one is good, two are better. The problem may be compounded by the use of bizarre, highly fortified health foods." The AAP Committee on Drugs specifically has urged the Food and Drug Administration to limit the potency of vitamin A preparations available over the counter.

There exists considerable information in the literature regarding these vitamins and their toxicity. A listing of a number of pertinent articles, many of them recent, regarding these vitamins has been placed on file with the Hearing Clerk, Department of Health, Education, and Welfare, Room 6–83, 5600 Fishers Lane, Rockville, Md. 20852 for public view.

The highlights regarding toxicity of vitamins A and D and the rationale for limiting over-the-counter availability of these vitamins are as follows:

VITAMIN A

Adverse effects which result from excess intake of vitamin A include anorexia, growth retardation in children, drying and cracking of the skin, hepatosplenomegaly, increase intracranial pressure, alopecia, migratory arthralgia, bone pain,

hypomenorrhea, irritability, and headache. Doses of 50,000 IU in adults and 20,000 IU in infants on a daily basis over long periods are known to produce toxicity. At present vitamin A is available over the counter in dosage levels as high as 50,000 IU per dosage unit. In recent years, some physicians and laymen have used large doses of vitamin A in the treatment of acne, although such therapy has not been shown to be safe and effective. Vitamin A in excessive dosages is used over long periods of time for this indication. Adverse effects, particularly increased intracranial pressure which may mimic a brain tumor, have been observed in children and young adults who are receiving vitamin A therapy for the treatment of acne. Reports of such effects have been published in the medical literature.

The position of the AAP on the matter is clear, as cited above.

In the United States, the Food and Nutrition Board, NAS/NRC, is the recognized authority for determining vitamin and other nutritional requirements for the human. The recommended daily dietary allowances (RDA) of the Food and Nutrition Board for vitamin A are 1,500 IU for infants; between 2,000 and 3,500 IU for children 1 to 9; between 4,500 and 5,000 IU for older children and adults; 6,000 IU during pregnancy, and 8,000 IU during lactation.

Based on the above considerations, it is the opinion of the Food and Drug Administration and medical experts that preparations containing vitamin A in excess of 10,000 IU per dosage unit shall be dispensed only by prescription and that for any vitamin A preparation intended for distribution as a dietary supplement or as an over-the-counter drug, the recommended daily dosage shall not exceed 10,000 IU vitamin A.

VITAMIN D

There are marked differences in tolerances to Vitamin D in humans when quantities in excess of normal requirements are ingested over prolonged periods. There are significant numbers of individuals who are hyperreactive to excess vitamin D. Generally, the margin of safety between nutritional requirements and toxic levels is small for vitamin D. The margin is particularly small in those individuals who are hyperreactive.

In infants, children and adults, excessive ingestion of vitamin D results in hypervitaminosis D characterized by anorexia, nausea, weakness, weight loss, polyuria, constipation, vague aches, stiffness, generalized vascular, soft tissue and premature epiphyseal calcification, nephrocalcinosis, hypertension, anemia, hypercalcemia, acidosis, irreversible renal failure and death.

Daily ingestion by infants of doses between 1,000 and 2,000 IU has produced hypervitaminosis D, usually manifested as the infantile hypercalcemia syndrome. There is good evidence suggesting that the supravalvular aortic stenosis syndrome with hypercalcemia in infants and children may result from excess intakes of vitamin D by the infant and/or by the mother during pregnancy. This latter syndrome may have a tragic outcome with severe aortic stenosis, mental and physical retardation, elfin facies, renal failure and death.

The recommended daily dietary allowance (RDA) of the Food and Nutrition Board, National Academy of Sciences-National Research Council of vitamin D for all age groups for which the vitamin is required is 400 IU. Although a daily intake of 400 IU of vitamin D is sufficient to prevent vitamin D deficiencies, preparations are available over the counter in dosage levels up to 25,000 IU per dosage unit. Excessive dosages of vitamin D have also been promoted in the lay press as noted above.

Based on the toxicity of vitamin D, the possibility of severe irreversible adverse effects in some instances, and the narrow margin of safety, it is the consensus of medical experts and the Food and Drug Administration that preparations containing vitamin D in excess of 400 IU per dosage unit shall be dispensed only by prescription and that the recommended daily dosage of any vitamin D preparation marketed as a special dietary food or as an over-the-counter drug shall not exceed 400 IU.

Therefore, because of the toxicity of vitamins A and D, their continued promotion in high doses to the lay person, and the continuing reports of adverse effects attributable to excessive intake of these vitamins, the FDA concludes it is in the interest of consumer safety to take the action herein described.

All vitamins are included among the over-the-counter drugs to be reviewed by an OTC Drug Advisory Review Panel, under the procedures established in the FEDERAL REGISTER on May 11, 1972 (37 F.R. 9464). Safety and effectiveness and more general questions related to adequate labeling of vitamin preparations marketed as OTC drugs will be considered by that panel, as well as the differences between foods for special dietary use, OTC drugs, and prescription drugs as they relate to vitamins. The Food and Drug Administration will publish, in the near future, new regulations governing dietary supplements of vitamins and minerals. Until such time as the OTC Drug Advisory Review Panel has completed its review and the new regulations for dietary supplements of vitamins and minerals are in effect, the Food and Drug Administration will not object to the inclusion in vitamin products marketed as foods for special dietary use or as OTC drugs of vitamin D at levels not exceeding 400 IU per dosage unit or 10,000 IU of vitamin A per dosage unit and with the recommended daily dosage not exceeding 400 IU of vitamin D or 10,000 IU of vitamin A.

Accordingly, pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (secs. 502 (a), (f), and (j), 503(b), 701(a), 52 Stat. 1050-1052, as amended, 1055; 21 U.S.C. 352 (a), (f), and (j), 353 (b), 371(a)) and under authority delegated to him (21 CFR 2.120), the Commissioner of Food and Drugs proposes to amend Part 3 by adding the following new sections:

§ 3.— Vitamin A preparations for oral use as drugs.

(a) Vitamin A is clearly known to be an essential nutrient for humans. Large doses of vitamin A can cause adverse effects, some of which are serious. The toxicity of vitamin A is well documented in the medical literature. The recommended daily dietary allowance (RDA) of the Food and Nutrition Board, National Academy of Sciences-National Research Council of vitamin A are: 1,500 international units (IU) for infants; between 2,000 and 3,500 IU for children 1 to 9; between 4,500 and 5,000 IU for adults; 6,000 IU during pregnancy, and 8,000 IU during lactation.

(b) In view of the toxicity from the use of large doses of vitamin A, the Food and Drug Administration finds that, in order to protect the public health, oral preparations containing vitamin A in excess of 10,000 IU per dosage unit are drugs subject to section 503(b)(1) of the Federal Food, Drug, and Cosmetic Act and shall be restricted to prescription sale. Such products will be regarded as misbranded if at any time prior to dispensing the following conditions are not met:

(1) The label bears the legend, "Caution: Federal law prohibits dispensing without a prescription"; and

(2) The labeling bears full disclosure information as required by § 1.106(b)(3)(i) of this chapter, and especially appropriate warnings regarding vitamin A toxicity.

(3) The recommended daily dosage of vitamin A does not exceed 10,000 IU.

(c) Vitamin A preparations labeled or dispensed contrary to this statement will be subject to regulatory proceedings as of (60 days after day of final promulgation in the FEDERAL REGISTER).

§ 3.— Vitamin D preparations for oral use as drugs.

(a) The importance of vitamin D in human nutrition is established. It is also widely recognized that vitamin D, when ingested daily in excessive amounts, is toxic. The recommended daily dietary allowance of vitamin D established by the Food and Nutrition Board, National Academy of Sciences-National Research Council for the prevention of vitamin D deficiency for all age and physiological groups for which the vitamin is required is 400 IU from all sources.

(b) In view of the known toxicity and seriousness of the adverse effects that may be caused by excessive consumption of vitamin D, the Food and Drug Administration finds that in order to protect the public health, oral preparations containing vitamin D in excess of 400 IU per dosage unit are drugs subject to section 503(b)(1) of the Federal Food, Drug, and Cosmetic Act and shall be restricted to prescription sale. Such products will be regarded as misbranded if at any time prior to dispensing the following conditions are not met:

(1) The label bears the legend, "Caution: Federal law prohibits dispensing without a prescription"; and

(2) The labeling bears full disclosure information as required by § 1.106(b)(3)(i) of this chapter, and especially appro-

priate warnings regarding vitamin D toxicity.

(3) The recommended daily dosage of vitamin D does not exceed 400 IU.

(c) Vitamin D preparations labeled or dispensed contrary to this statement will be subject to regulatory proceedings as of (60 days after day of final promulgation in the FEDERAL REGISTER).

Interested persons may, within 60 days after publication thereof in the FEDERAL REGISTER, file with the Hearing Clerk, Department of Health, Education, and Welfare, Room 6-88, 5600 Fishers Lane, Rockville, MD 20852, written comments (preferably in quintuplicate) regarding these proposals. Comments may be accompanied by a memorandum or brief in support thereof. Comments received will be available for public inspection at the above office during regular business hours, Monday through Friday.

Dated: November 28, 1972.

CHARLES C. EDWARDS,
Commissioner of Food and Drugs.

[FR Doc.72-21379 Filed 12-13-72;8:45 am]

DEPARTMENT OF HOUSING AND URBAN DEVELOPMENT

Office of Assistant Secretary for Housing Production and Mortgage Credit—Federal Housing Commissioner (Federal Housing Administration)

[24 CFR Part 201]

[Docket No. R-72-225]

PROPERTY IMPROVEMENT AND MOBILE HOME LOANS

Notice of Proposed Rule Making

The Department of Housing and Urban Development is considering amending Part 201 of Title 24 of the Code of Federal Regulations, Subpart B, "Mobile Home Loans". The amendments issued in accordance with section 2(a) of the National Housing Act, 12 U.S.C. 1701, would permit acceptance of a used mobile home in lieu of the minimum required cash downpayment where the bluebook value of the mobile home being offered as a trade-in is equal to or greater than the minimum cash downpayment. This amendment would permit savings to consumers as the sales tax on the new mobile home being purchased in some cases would be reduced by an amount equivalent to the tax on the value of the trade-in. The second amendment would permit insured lenders to accept a financial statement from a mobile home dealer that has been prepared by a licensed public accountant. This change is necessary as the requirement of certification of financial statements has proved to be an undue burden on small businesses which ordinarily do not have their books certified.

All interested persons are invited to submit written comments or suggestions in triplicate with respect to this proposal, on or before January 16, 1973, addressed to the Rules Docket Clerk, Office of the General Counsel, Room 10256, Department of Housing and Urban Development, 451 Seventh Street SW., Washington, DC 20410. All relevant material will be considered before adoption of a final rule. A copy of each communication will be available for public inspection during regular business hours at the above address.

The proposed rule is issued pursuant to section 7(d) of the Department of Housing and Urban Development Act, 42 U.S.C 3535(d).

Part 201 is proposed to be amended as follows:

1. Section 201.535 is amended to read:

§ 201.535 Borrower's minimum investment.

The borrower shall make a minimum cash downpayment of at least 5 percent of the first $6,000 of the total cost of the mobile home as shown in the purchase contract (excluding permissible charges and fees provided for in § 201.530(b)) plus 10 percent of any amount in excess of $6,000. A used mobile home with a blue-book value equal to or greater than the required minimum downpayment may be accepted in lieu of a cash downpayment.

2. Section 201.595(b) is amended to read:

§ 201.595 Dealer investigation, approval, and control.

* * * * *

(b) *Financial statement required.* The insured shall obtain a financial statement of the dealer, prepared by a licensed public accountant, not less than once every 12 months. If no loans have been purchased, prior to the date of such financial statement, the insured shall approve the dealer as provided in paragraph (a) of this section.

* * * * *

Issued at Washington, D.C., December 8, 1972.

EUGENE A. GULLEDGE,
Assistant Secretary for Housing Production and Mortgage Credit—Federal Housing Commissioner.

[FR Doc.72-21523 Filed 12-13-72;8:51 am]

DEPARTMENT OF TRANSPORTATION

Coast Guard

[46 CFR Part 10]

[CGD 72-132PH]

UNINSPECTED TOWING VESSELS

Licensing of Operators; Extension of Time for Comments

In the August 11, 1972, issue of the FEDERAL REGISTER (37 F.R. 16374), the Coast Guard proposed regulations governing the issuance of licenses for the operation of uninspected towing vessels to implement the Towing Vessel Operator Licensing Act, Public Law 92-339, 1t.S. 4427, as amended, 46 U.S.C. 405(b) (July 7, 1972).

Public hearings on the proposed regulations were held in Seattle, Wash.; New York, N.Y.; New Orleans, La.; and St. Louis, Mo. In addition, interested persons were given until October 17, 1972, to submit comments. The Coast Guard subsequently received requests for extension of this period to allow interested individuals and organizations to fully document comments submitted. These requests were considered justified and extensions were granted until November 30, 1972.

Among the comments received during the last extension, several addressed themselves to the question of terminology on the license issued, i.e., whether to call the person an Operator or Second Class Operator as proposed or whether a different title such as the more traditional Master or Mate should be used.

Since these recently received comments on this subject, if adopted, could be considered a substantive change to the regulations as proposed, the Coast Guard feels that an additional extension is warranted. This will allow the public to fully participate in the rule making process and give all interested parties an opportunity to express their views on this issue.

In view of the above, the Coast Guard hereby extends the period for such comments to January 15, 1973. All relative comments received by that time will be considered.

Interested persons may participate in this proposed rule making by submitting written data, views, or arguments to the Executive Secretary, Marine Safety Council (GCM/82), Room 8234, 400 Seventh Street SW., Washington, DC 20590, phone: 202—426-1477. Written comments should include the docket number (CGD 72-132PH), the name and address of the person submitting the comments, and the section of the proposal to which each comment is directed. Copies of comments received will be available for examination in Room 8234, 400 Seventh Street SW., Washington, DC.

Dated: December 8, 1972.

W. F. REA, III,
Rear Admiral, U.S. Coast Guard, Chief, Office of Merchant Marine Safety.

[FR Doc.72-21519 Filed 12-13-72;8:50 am]

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IN THE MATTER OF

PROPOSED STATEMENT OF POLICY
CONCERNING VITAMIN A AND VITAMIN D

OBJECTIONS & COMMENTS OF THE NATIONAL NUTRITIONAL FOODS ASSOCIATION

TO: Dr. Charles C. Edwards,
Commissioner of Food & Drugs
Department of Health, Education
& Welfare
Food & Drug Administration

Sir:

The following comments are respectfully submitted on behalf of the National Nutritional Foods Association with respect to the Proposed Statement of Policy converning Vitamin A and Vitamin D published in the Federal Register on December 14, 1972 (21 CFR Part 3).

The National Nutritional Foods Association is composed of business concerns, located throughout the United States, engaged in the manufacture, distribution and sale of vitamins and dietary supplements. These business concerns include manufacturers, wholesalers and retailers all of whom have a vital interest in the limitations set forth in the Commissioner's Proposed Statement of Policy. These comments are submitted on behalf of the Association and the consumers whose freedom

of choice in the selection of these Vitamins would be unduly and unjustifiably restricted by the implementation of the proposals herein considered.

By the instant proposal, the Commissioner would add two new sections to Part 3 of Title 21 of the Code of Federal Regulations. The first of these sections would declare that any vitamin preparation containing in excess of 10,000 I.U. of Vitamin A is a drug restricted to prescription sale. The second section similarly would declare that any vitamin product containing in excess of 400 I.U. of Vitamin D is a drug restricted to prescription sale. It is respectfully submitted that these limitations are without scientific foundation, are beyond the intent of the provisions of the Federal Food, Drug and Cosmetic Act and constitute an unwarranted interference with the right of the consumer to obtain these ingredients without the burden and expense of prescription limitation.

It is essential to first determine what it is that is here being considered. We are not discussing any matter of drugs of chemicals, but rather common food ingredients. The substances here considered are constituents of common food items such as liver, carrots, spinach and the like as to which there has never been any question of danger or toxicity.

The purported reason behind the present proposal to require prescriptions for Vitamin A in excess of 10,000 I.U. and Vitamin D in excess of 400 I.U. is that there is a danger of toxicity in the inges-

tion of these vitaimins in amounts exceeding those levels. It is asserted, in the Proposed Statement of Policy, that this "danger" of toxicity is well documented in the medical literature. An evaluation of the medical comments and the 9 page listing of this so called literature filed with the Hearing Clerk demonstrates, however, a total lack of support for the arbitrary limitations being proposed herein.

The June 1, 1972 Newsletter comment of the American Academy of Pediatrics (A.A.P.) referred to by the Commissioner (p. 26618 of the Federal Register) is the first example of the inapplicability of these medical references to the present proposal. This comment insofar as it refers to toxic effect, does so solely in terms of infants and children. Moreover, the article specifically purports to be a response to the press, radio and television recommendations of nutritionist Adelle Davis. The A.A.P. comment cites an article written by Miss Davis. That article does not, however, make recommendations directed towards infants and children. Miss Davis' article is clearly in the context of adults. It refers to airplane pilots, automobile drivers and specifically uses herself and the term "adults" in stating her views and recommendations. We submit this A.A.P. comment on toxic effects in infants and children cannot in any way be considered as substantive support for the instant proposal which would require adults desiring to obtain a Vitamin A supplement of anything over 10,000 I.U. to get a prescription.

The nine page bibliography amply demonstrates that there is no basis for prohibiting the sale of Vitamin A and D without prescription at the levels above 10,000 I.U. and 400 I.U. Of the 70 references pertaining to Vitamin A (pages 1 through 6) of the bibliography 53 are dated 1967 and before. Of the 38 references pertaining to Vitamin D, (pages 7 through 9 of the bibliography) 31 are also dated 1967 and before. Thus 84 of the 104 references relied upon to support the danger of toxicity which is the purported basis for the proposed limitations were published before the Food and Nutrition of the National Research Council, National Academy of Sciences published its Recommended Dietary Allowances, Seventh Edition, 1968. At the time when the overwhelming majority of the reports in the Vitamin A bibliography were available, the Food and Nutrition Board stated at page 23 of its publication, "If large doses of Vitamin A (20 to 30 times RDA) or of carotene are ingested for long periods of time, manifestations of toxicity develop." The RDA referred to is of course 5,000 I.U. per day. Thus, the Food and Nutrition Board speaks of manifestations of Vitamin A toxicity at levels of 100,000 to 150,000 I.U. ingested for long periods of time. Considering infants, for whom the RDA is 1,500 I.U. per day, the Food and Nutrition Board noted that the level for toxic resultsis at daily levels of 18,000 units for one to three months.

Considering Vitamin D toxicity, the same Food and Nutrition Board reported at pages 25 and 26 of its 1968 publication that generally "potentially dangerous" levels of Vitamin D were at levels " of the

order of 1,000 to 3,000 I.U./Kg/day" and that "there is no evidence that intakes of the order of 2,000 to 3,000 I.U./day produce hypercalcimia beyond infancy."

It is thus obvious that notwithstanding the reports set forth in the bibliography used to support the present proposal, the Food and Nutrition Board has considered the problem of toxicity at levels far beyond the arbitrary and unreasonable low levels for which prescription requirements are now being suggested. This is the same Food and Nutrition Board, NAS/NRC which the Commissioner has stated in his notice of the instant proposal to be "the recognized authority for determining vitamin and other nutritional requirements for the human" (pg. 26619 Federal Register, Dec. 14, 1972). Moreover, the Commissioner has described the Food and Nutrition Board's 1968 RDA publication as a "source of authentic and reliable information on which to base recommended daily allowances of nutrients (Proposed Finding of Fact No. 9 in Tentative Order concerning 21 CFR Part 125, Special Dietary Use). Surely then, the Food and Nutrition Board's 1968 publication is a recognized authority and source of authentic and reliable information concerning the levels at which there may be a question of Vitamin A and D toxicity.

A review of a substantial portion of the individual reports listed in the bibliography filed with the Hearing Clerk, establishes that the levels of Vitamin A and D wherein a question of hypervitaminosis may arise are far beyond the 10,000 I.U. and 400 I.U. restrictions now being considered. Most of these reports were available when the

Food and Nutrition Board made its findings on the subject, and those articles which appeared afterwards add nothing to the information available to the Board when it published its findings and conclusions.

Considering the articles on Vitamin A teratogenicity we find generally that they deal with animal studies. One study (No. 10, page 1 1960) dealt only with hypovitaminosis instead of the hypervitaminosis which is the subject of the proposed statement of policy. The reports of Warnaky, Wilson, Cohlan and Seward (Nos. 1,3,6, and 17 pages 1 & 2, 1940, 1949, 1953 and 1966) dealt with rats. The Wilson report again was a Vitamin A deficiency study. The two reports by Kalter (Nos. 11 & 12 page 1 - 1960 & 1964) the report by Ferm (No. 14, page 1 - 1965) and the report by Murakami (No. 15, page 2 - 1965) involved studies on mice. Dogs (beagle bitches) receiving daily doses of 50,000 - 125,000 I.U. of Vitamin A were the subject of the Wiersig report (No. 18 page 2 - 1967). Hamsters treated with 75,000 to 400,000 USP units of Vitamin A per Kg body weight and guinea pigs treated with 200,000 units per Kg were reported by Robins (No. 21, page 2 - 1970). Robins reported that these levels were up to several hundred times the minimum daily requirement of each species. Considering the teratogenic effect of these exceedingly high doses of Vitamin A, Giroud (No. 7, page 1 - 1968) noted this action differs with different species, rats and mice being much more sensative than guinea pigs and rabbits. Giroud noted "Vitamin A does not seem to be teratogenic in humans." The most recent report cited

in the bibliography by Shenefelt, 1972 (No. 10, page 2) again observes that these animal studies involve dosages which are hundreds of times the daily requirements.

One of the few human studies in the Vitamin A teratogenicity bibliography involved a daily dosage of 150,000 units of Vitamin A administered to 10 adults for 30 days (Pinkus, No. 1, pg. 1 - 1964). This is at a level 30 times the RDA. Nowhere in the bibliography under Vitamin A teratogenicity do we find any support for restricting the sale of Vitamin A without prescription to 10,000 I.U. The following table demonstrates that an analysis of the Vitamin A toxicity bibliography leads to the same conclusion - the reports concern massive doses of Vitamin A of a magnitude nowhere near the 10,000 I.U. limitation being proposed:

ANALYSIS OF LEVELS OF VITAMIN A TOXICITY REPORT IN FDA BIBLIOGRAPHY

Reference No. and Author	Year	Age of Subject	Vitamin A Dosage	Time Period
(1) Josephs	1944	Infant (34 Mos)	240,000/day	31 mos.
(2) Toomey	1947	Infant (2 yrs)	6,200,000	14 days
(6) Wyatt	1950	3 years	400,000-500,000/day	2 years
(8) Sulzberger	1951	44 years	600,000/day (supplemented by occassional doses of 1,000,000 to 2,000,000 units per day)	18 mos.
(10) Bair	1951	1 yr 4 mos	240,000/day	3 mos.

Reference No. and Author	Year	Age of Subject	Vitamin A Dosage	Time Period
(12) Goldzier	1952	2 yrs.	(5,000/day	2 mos.
			(7,500/day	4 mos.
		(History of one patient)	(12,500/day	11 mos.
			(150,000/day	4 mos.
			(300,000/day	2 mos.
(13) Bifulco	1953	52 yrs.	100,000/day	4 yrs.
(14) Shaw	1953	25 yrs.	200,000-275,000/day	2 mos.
(16) Gerber	1954	Adult	500,000/day	8 yrs.
(Reports of other authors)		4 Adults	200,000	single dose
		?	50,000-100,000/day	2 yrs.
		?	150,000/day	2 mos.
(17) Tudor	1955	20 mos.	200,000/day	8 mos.
(18) Pickup	1956	6 yrs.	450,000/day	6 wks.
		4 yrs.	325,000/day	2 yrs.
(19) Elliott	1956	21 yrs.	150,000/day	7 mos.
(20) Oliver	1958	14 yrs.*	200,000/day	10 mos.
		Also review of other reports of Vitamin A intoxication (27 infants, 3 children & 6 adults) at levels up to 600,000/day and dose duration to 8 1/2 yrs., ranging from 20 to 400 times the RDA except for one 1955 report of 50,000/day for 3 yrs. by 51 yr. old man.		
(21) Oliver	1958	14 yrs.*	200,000/day	10 mos.
(22) Morrice	1960	14 yrs.*	200,000/day	10 mos.
		15 yrs.	200,000/day	?
		16 yrs.	90,000/day	3 1/2 yrs.
(24) Stimson	1961	32 yrs.	100,000/day	5 yrs.
(Reports of other authors)		54 yrs.	50,000/day	3 yrs
		44 yrs.	1,000,000/day	two occassions 14 and 25 days respectively

*/ Same 14 year old subject.

Reference No. and Author	Year	Age of Subject	Vitamin A Dosage	Time Period
(26) Pease	1962	Infants (7 cases - but no Vit. A determination made in one)	Dosage and time unspecified but conclusion that "the statement that 200,000 units of Vitamin A may be given to a child each day with impugnity appears to be erroneous."	
(27) Sober-Beckara	1963	39 yrs.	75,000-150,000/day 375,000/day for...	8 yrs. then 5 mos.
(30) Bergen	1965	62 yrs.	41,000/day(?)	8 yrs.
(32) Silverman	1965	6 Adults (33 to 80 yrs)	600,000/day	5 wks.
(33) Turtz	1960	17 yrs.	200,000/day	18 mos.
(35) DiBenedetto	1967	51 yrs.	600,000/day	3 yrs.
(36) Muenter	1971	18 yrs. 52 yrs.	100,000-200,000/day 200,000-300,000/day	18 mos. 8 yrs.
(37) Feldman	(1970)	20 yrs. 20 yrs.	100,000-500,000/day 100,000/day	4 yrs. 3 1/2 yrs.
(38) Fedotin	(1970)	18 yrs.	150,000/day	4 yrs.
(39) Nater	1970	11 Adult Fishermen	2,000,000-30,000,000 (20-300 gms halibut liver)	Single dose
(40) Rubin	1970	6 yrs.	400,000-625,000	4 1/2 yrs.
(41) Morrice	1971	Letter to editor which merely refers to reports by Oliver & Morrice which are already listed at Nos. 21 and 22 above.		
(42) Gelpke	1971	15 yrs.	200,000/day	2 yrs.
(43) Weiland	1971	16 yrs.	105,000-305,000/day	6 mos.
(44) American Academy of Pediatrics	1971	Contains footnote references most of which are to a number of the studies reviewed in this table		

The foregoing analysis shows that the bibliography filed with the Hearing Clerk fails to support the drastic and unwarranted require-

ment that Vitamin A in excess of 10,000 I.U. be available only on prescription. Even at the high levels used in these reports, the symptoms which followed were generally found to disappear when such use was discontinued. The reports in this bibliography, including those of recent vintage, overwhelmingly deal with instances of daily intakes of millions or hundreds of thousands of units of Vitamin A over prolonged periods of time. In the one study where there is a report of a case as low as 41,000 units (No. 30, Bergen - 1965) the author noted that the patient's neurotic state may have interfered with her ability to relate her actual daily intake which the author implies may have been higher. Dr. Fedotin in the April 27, 1970 issue of the Journal of the American Medical Association (No. 37 in the bibliography) states that the smallest dose of Vitamin A reported to produce symptoms in an adult is 50,000 units given over an 18 month period. As indicated in the above table, the reports at the 50,000 level are few and far between those of the massive doses which make up the bibliography of Vitamin A toxicity reports. Signigiantly, all the reports concerning 50,000 units predate the Food and Nutrition Board's conclusion that manifestations of toxicity develop at 0 to 30 times the RDA.

The Vitamin D bibliography furnished in support of the 400 I.U. limitation is likewise lacking of persuavsiveness in support of the arbitrary limitation sought to be imposed. As heretofore noted, most of this literature was available before the Food and Nutrition Board's statement in 1968 fixing toxicity levels far beyond 400 I.U. In the Barnes report of 1957 (No. 5 in the Vitamin D bibliography) a 67 year old

patient took 300,000 I.U./day for 3 months or more. Barnes also reported that the shortest time reported for Vitamin D toxicity was 12 days at 750,000 I.U./day. The Hass report (No. 7 - 1958) involved a rabbit study where the authors reported that the minimal conditions for the production of calcinosis were a duration of eight days and a total of 3,000,000 units given in three equal doses at intervals of two days.

In the DeWind report (No. 12 - 1961) a 3 year old boy was given 100,000 units/day plus 2 tablespoons of cod liver oil and multivitamin drops, for 8 months. Taylor (No. 19 - 1966) reported a 41 year old man receiving 200,000 units by injection three times weekly for three weeks. Stickler's report of "Possible Detrimental Effect..." (No. 25 - 1971) told of twins who received up to 800,000 I.U./daily. But this report also stated "There were no episodes of clinically recognized Vitamin D intoxication." The West study (No. 26 - 1971) noted that 25,000 to 75,000 I.U. daily is a range which rarely results in intoxication.

Not only do the reports in this bibliography indicate that toxicity occurs at levels many times the RDA of Vitamins A & D, but several reports demonstrate a lack of toxicity at high dosage levels. Josephs (No. 1 Vitamin A bibliography), for example, cited the observation of an eight month old infant who received 500,000 units of Vitamin A daily over a period of over four months with no symptoms of toxicity and with a normal blood vitamin A level. The 52 year old woman reported by Meunter et al. (No. 36) showed no signs of toxicity when she took 100,000 I.U. Vitamin A daily for three months. Gerber (No. 16) reported two patients

who took 25,000 to 50,000 units of Vitamin A for six years and had no complaints referable to possible vitamin A toxicity. Krause reported the case of a 79 year old man who had taken 50,000 I.U. of Vitamin A, because he thought it was good for him, without any signs or symptoms of Vitamin A toxicity. (No. 6 - Amer. J. of Clinical Nutrition, June, 1965). Krause stated:

> "From a nutritional point of view, it is interesting that the ingestion of this excessive amount of vitamin A for seventeen years did not produce any well recognized signs and symptoms of toxicity."

Standard medical texts likewise demonstrate the absence of any reasonable relationships between the proposed prescription levels of Vitamins A and D and the intake levels which result in the toxic syndrome known as hypervitaminosis. Goodman and Gilman in their leading text, The Pharmacological Basis of Therapeutics, (4th Ed., 1970) note at page 1674 that the reported cases of hypervitaminosis A in children have been associated with the chronic ingestions of from 50,000 to 500,000 units per day (the RDA for infants and children is from 1,500 to 3,500 units per day). Concerning Vitamin D, Goodman and Gilman state at page 1684:

> "There is wide individual variation in the amount of Vitamin D that causes hypervitaminosis. As a rough approximation, it may be stated that the continued ingestion of 150,000 units or more daily by a person with normal vitamin D sensitivity may result in poisoning."

Similarly, the Merck Index (12th Ed., 1972) makes the following observa-

tions as to hypervitaminosis A:

> "Acute toxicity in children has resulted from large doses (several hundred thousand U.S.P. units)... Arctic explorers, on ingesting several million Units of Vitamin A in polar bear or seal liver, have developed drowsiness, irritability, headache, and vomiting a few hours later, with subsequent peeling of the skin.
> Chronic poisoning in older children and adults develops, usually, after doses of 100,000 U.S.P. u./day for many months. It has been shown that infants may develop evidence of toxicity in a few weeks with a dosage of 20,000 to 60,000 u./day of water-dispersible vitamin A."

The same recent edition of the Merck index gives the following information as to hypervitominosis D:

> "Vitamin D 40,000 U.S.P. u./day produces toxicity within one to four months in infants: toxic effects have been observed in adults receiving 100,000 u./day for several mo."

The introductory comments to the proposed statement of policy contains several remarks as to overzealous use of Vitamin A by parents and the use of "bizarre highly fortified health foods." We respectfully submit that the mere fact that some people fail to follow the directions for daily use that appear on every vitamin product is not a basis for imposing prescription requirements on non-toxic levels of an ordinary vitamin. If this approach were followed to its natural conclusion, then we should put all OTC products on prescription. The simple 5 grain aspirin product is a drug whose actions are not fully understood; it is a product every bit as prone to the "popular premise" referred to in the Statement of Policy "that if one is good, two are better." Yet

pirin is not a prescription item. Nor are we suggesting that it ould be. But by the same token, it is not too much to suggest that mple vitamin products should be accorded the same treatment. To the tent that a question of overzealous use may exist as to infants and ildren, proper cautionary statements may be appropriate. Indeed, the gulations concerning dietary supplements for infants have been imple- nted without any question as to the levels of Vitamins A and D fixed ereon. We submit, however, that there is no need or basis to prohibit ults from exercising their freedom of choice in the foods and supple- nts that they eat without having to go to a doctor to get a prescrip- on. The presecription requirement for Vitamin A above 10,000 I.U. is t supported by the reports and studies in the medical literature. tamin A deficient diets are not uncommon in this country. To require hysician's presecription for ordinary dietary supplements, imposes high ts and expenses upon the consumer without just cause.

The natural extension of the instant proposal would be to place hibitions upon the ordinary foods we eat and require prescriptions for rots, milk, liver and other common foods. Thus, the United States artment of Agriculture in its Handbook No. 8, "Composition of Foods" ws that ordinary foods contain large amounts of Vitamin A as follows:

Food	Units per 100 gms (3.3 oz.)
Raw Carrots	11,000 I.U.
Raw Beef Liver	43,900 I.U.
Pumpkin Pie	2,400 I.U.
Raw Sweet Potatoes	8,800 I.U.
Spinach	8,100 I.U.

lowing the position of the FDA in the Proposed Statement of Policy its logical conclusion, the butcher would require a prescrip-

tion for the sale of his liver, the vegetable man would require a prescription to sell his carrots and the baker would require a prescription to sell his pumpkin pies. Such a conclusion is obviously irrational and is not a fulfillment of the Congressional direction under the Statute.

The National Nutritional Foods Association is very much concerned about the reference to the health food industry in the Proposed Statement of Policy. It has been shown herein that the medical literature fails to support the imposition of prescription limitations at levels anywhere near those being suggested. Are we then to conclude that the instant proposal is but an oblique attack by FDA on the industry and the millions of consumers who desire to exercise their freedom of choice in selecting the foods they eat by purchasing food at a local health food center. The subject of dosage levels of dietary supplements has been a matter of serious controversy in considering FDA's extensive efforts to change its regulations on foods for special dietary use and impose standards of identity for vitamin supplements. The awesome specter of toxicity as to Vitamin A and D casts an unwarranted cloud over the consideration of these ingredients in the dietary supplement regulations. The present proposal for prescription requirements for Vitamins A and D obviously limits the consideration of objections to the restrictions on these ingredients in the proposed regulations concerning vitamins and dietary supplements just recently announced by FDA. Analysis of the bibliography concerning Vitamins A and D makes clear that no question of

harm or safety exists as to these ingredients at levels far beyond those for which a prescription would be required. The instant proposal should, therefore, not be allowed to interfere with a full consideration of all ingredients effected by the pending dietary supplement regulations.

Finally, we respectfully submit that the instant proposal is beyond the legal authority of the Commissioner in that it is not within the intent of the applicable provisions of the Food and Drug Act. The Vitamins effected by the instant proposal are recognized as safe at levels many times those of the RDA. The U.S. Pharmocopia, recognized as an official compendium of drugs by the Food and Drug Act, lists 25,000 as the usual therapeutic dose of Vitamin A and 25,500-200,000 as the usual dose range. No suggestions are made that a prescription be required at even those levels, let alone any lower levels. It is not the intent of the statute that ordinary food items be converted into prescription drugs simply because some people may exceed the recommended daily dosage thereof. Clearly these ingredients are safe for use without the supervision of physicians at levels far above those presently proposed. To the same effect we could consider salt or even water as dangerous in high levels. Yet no one has ever suggested that these foods be considered prescription items. Clearly the food substances here under consideration do not fall within the provisions of Section 503(b) of the Statute.

The sale of vitamins and food supplements has been governed by regulations in effect since 1941. There is no need now to suddenly remove from the market place vitamins and food supplements which have been

available to the American consumer for over 30 years subject to these regulations. No emergency or iminent threat of danger has been shown to exist to justify the economic hardships which would be imposed upon manufacturers, distributors, retailers and the consumer alike by the sudden and arbitrary prohibitions suggested in the proposed Statement of Policy. The prohibitions are unnecessary, unjust, arbitrary and beyond the purpose and intent of the law.

Conclusion

The Proposed Statement of Policy requiring a doctor's prescription for oral preparations containing Vitamin A in excess of 10,000 I.U. per dosage unit and Vitamin D in excess of 400 I.U. per dosage unit is manifestly unsound, arbitrary and unreasonable. The very medical literature relied upon by the Food and Drug Administration demonstrates that there is no question of safety or harm in daily intakes of these ingredients, at levels many times the restrictive and arbitrary limitations now being proposed. The present law and regulations provide ample means for furnishing relevant information concerning vitamins and food supplements without imposing unnecessary, unreasonable and illegal prohibitions upon the consumer's freedom of choice in the selection of the foods he eats.

Dated: New York, New York
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FAT-SOLUBLE VITAMINS

VITAMIN A AND CAROTENE

Vitamin A in the human diet derives from preformed vitamin A and from provitamin A carotenoids. Of the latter, β-carotene is the most important, having the highest vitamin A activity and being the most plentiful carotene present in many important human foods. Carotenes are active only after being converted into vitamin A during or subsequent to absorption through the intestinal wall. One international unit (IU) of β-carotene (0.6 μg all-*trans* β-carotene) is equivalent to one IU of vitamin A [0.3 μg all-*trans* vitamin A alcohol (retinol) or 0.344 μg all-*trans* vitamin A acetate (retinyl acetate)] in the rat.[1] There is no evidence that these same potency relationships do not apply to humans.[2] However, the availability of carotenes in foods as sources of vitamin A for humans is low and extremely variable. Often, factors of 1/2, 1/3, 1/4, or less are arbitrarily used to compensate for this lower availability of carotenes from different foods.

Food-composition tables should show both the β-carotene and the vitamin A content of foods, but one should be aware that other isomers of carotene and vitamin A occur in foods and that these have less vitamin A potency than do their all-*trans* forms. The predominant forms of carotene and vitamin A in nature have the all-*trans* configuration. However, each of the principal carotenoids (α-, β-, and γ- carotenes and cryptoxanthin) is capable of existing (or being formed during heat processing and cooking) in a number of stereoisomeric forms having widely different potencies. Similarly, the vitamin A stereoisomers with *cis*-configurations are less potent than all-*trans* vitamin A. Development and use of analytical methods for evaluating all the various vitamin A-active compounds in foods are needed.

The functions of vitamin A in the body are not completely understood. Its role in the visual process is established best. A specific vitamin A aldehyde (9-*cis*-retinaldehyde) is essential for the formation of rhodopsin and the normal functioning of the retina. A vitamin A-deficient animal has impaired dark adaptation, and measurement of this defect is a common method for studying vitamin A requirement in humans. Vitamin A also participates in the maintenance of the integrity of the epithelial membranes. Stratified keratinizing epithelium is substituted for normal epithelium in the eyes and paraocular glands and in the respiratory, alimentary, and genito-urinary tracts, for example. The common deficiency symptoms are increased susceptibility to microbial infections, xerophthalmia and other eye disorders, loss of appetite and weight, and sterility. There are indications that vitamin A plays a fundamental role at the cellular level and maintains the integrity of the mucopolysaccharide structure of the cell.[3]

Few experiments have been conducted to determine the minimum daily requirement of human adults, and these have involved few subjects. The most widely accepted value resulted from a study conducted by the Medical Research Council in Great Britain,[3] wherein it was suggested that 1,300 IU/day represented the minimum protective dose, based on changes in scotopic vision. This dose was inadequate to maintain blood vitamin A levels and thus would not have maintained liver stores. Animal studies[4-6] have shown that, in the absence of specific factors influencing vitamin A mobilization or transport, significant deposition of vitamin A in the liver does not occur until blood concentrations approach "normal." It was concluded that 2,500 IU of preformed vitamin A per day represented the adult requirement. The FAO/WHO report on vitamin A requirements recommends an intake of 2,500 IU and assumes that the availability of β-carotene is one third and the efficiency of conversion of the available β-carotene is one half. Therefore, on a weight basis, the over-all utilization efficiency of β-carotene is one sixth of that of vitamin A.[7]

However, in most diets, the vitamin A intake is derived both from the preformed vitamin and from carotene with lower availability than that of the preformed vitamin. Therefore, for a mixed diet, the recommended intake of vitamin A should be adjusted upward.

In the United States, the usual foods available are estimated to provide about 7,500 IU of vitamin A per day: about 3,500 IU derived from vegetables and fruits; 2,000 IU from fats, oils, and dairy products; and 2,000 IU from meat, fish, and eggs.[8,9] Thus, about one half of the apparent vitamin A intake is in the form of the provitamin.

For the reference man and woman, the RDA is set at 5,000 IU of vitamin A. For practical purposes, within the United States, it is not considered to be necessary to further adjust the RDA of 5,000 IU for variations in the proportions of preformed vitamin A and provitamin A in the diet.

Since few studies have been conducted on the vitamin A requirement of human infants, the RDA for this age group is deduced from the fact that human milk apparently supplies adequate vitamin A for good health during the first year of life. Human milk has a vitamin A content of 170 IU/100 ml. Assuming consumption of approximately [illegible] ml of human milk, the infant would receive about 1,500 IU, and [illegible] is taken as the RDA.[10]

Investigations are needed to establish the requirements for vitamin A during childhood, adolescence, and other periods when growth spurts normally occur. In their absence, only interpolated estimates of allowances, as shown in the table, can be made for boys and girls of different ages, based on average body weights, plus additional arbitrary amounts to satisfy growth needs.

About 1,000 IU/day additional vitamin A should be provided during the latter two thirds of pregnancy, since the nutritional well-being of the rapidly growing fetus is dependent on the mother's intake of this vitamin. To help ensure the nursing infant ample amounts of vitamin A, an additional 3,000 IU is recommended during lactation.[8,11]

If large doses of vitamin A (20 to 30 times RDA) or of carotene are ingested for long periods of time, manifestations of toxicity develop.[12,13] Carotene in massive doses is not converted to vitamin A rapidly enough to induce vitamin A toxicity, but the excess carotene accumulates in the body without producing clinical symptoms other than yellow skin. This quickly returns to normal when carotene ingestion is stopped. Ingestion of excess vitamin A is more serious. Symptoms of excessive intake include anorexia, hyperirritability, skin lesions, bone decalcification, and increased intracranial pressure. Doses as low as 18,500 IU of a water-dispersed vitamin A–D preparation daily for one to three months are reported to be toxic for infants three to six months of age.[14]

Many factors influence vitamin A requirements. For example, some dietary fat is needed for absorption of vitamin A. Protein malnutrition, however, results both in decreased intestinal absorption and in impairment of blood transport of vitamin A. As with all the fat-soluble vitamins, normal functioning of the gastrointestinal tract, especially bile secretion, is essential for absorption of vitamin A. Laxa-

tives, antibiotics, and certain other drugs decrease the absorption of vitamin A from the intestinal tract, as do various disease states, such as celiac disease and other malabsorption syndromes.

VITAMIN D

Vitamin D is essential at all ages for maintenance of calcium homeostasis and skeletal integrity. Vitamin D can be acquired by ingestion of vitamins D_2 (ergocalciferol) or D_3 (cholecalciferol) and by exposure to certain ultraviolet wavelengths of light, which convert 7-dehydro-cholesterol in the skin to vitamin D_3. Vitamin D deficiency can occur only when the amount supplied by both sources is inadequate. One international unit of vitamin D is 0.025 μg of pure vitamin D_3.

Requirements and Recommended Allowances at Various Ages

The requirement for vitamin D can be met entirely by skin irradiation, so that the need for ingested vitamin D is influenced by the amount of exposure to ultraviolet light. There are few reliable data concerning minimum vitamin D requirements, except for infants. However, long experience has shown that 400 IU/day are sufficient to meet the requirements of practically all healthy individuals, assuming no exposure to ultraviolet light. There is also good evidence that such intakes are nontoxic. The allowances recommended during infancy are well documented [1]; however, those recommended for children and adolescents and during pregnancy and lactation are not well documented and may exceed actual requirements.

In normal full-term infants, intakes of as little as 100 IU/day have prevented rickets.[2-4] Actively rachitic infants have been cured with 300 IU/day.[2] With inadequate vitamin D intake, prematurely born infants develop rachitic lesions more readily than full-term infants, because of their more rapid growth rate. However, the administration of as little as 100 to 200 IU daily has been adequate to prevent biochemical evidence of rickets and to sustain normal skeletal growth in premature infants ingesting adequate amounts of calcium and phosphorus.[5,6] Assuming a satisfactory calcium intake, the ingestion of 400 IU/day provides for excellent skeletal growth, promotes satisfactory

calcium absorption and metabolism, and prevents rickets in practically all normal full-term and premature infants.[1-6,7]

Vitamin D is required throughout the growth period, as evidenced by the rare occurrence of vitamin D-deficiency rickets in adolescents.[8] However, the requirement has been more difficult to determine beyond infancy, because of the greater access to sunlight and various food sources of vitamin D, and because skeletal changes occur less rapidly. In the past, the recommended intake for children and adolescents has been 400 IU/day,[1,9,10] and this is reaffirmed here. Ingestion of this amount of vitamin D protects practically all normal children from deficiency, and there is no evidence that this intake is harmful in any way.[1]

Diet surveys indicate that the majority of adolescents[11,12] do not take vitamin supplements. Because of inconsistency in the addition of vitamin D to commercial foods in North America (in Canada, until very recently, fortification of fluid milk was not permitted), many such individuals ingested much less than 400 IU of vitamin D per day, the total oral intake from all sources amounting to less than 100 IU/day in a number of instances.[13] Despite this, the general health and growth of these individuals were satisfactory. Furthermore, clinical rickets owing to vitamin D deficiency is virtually unknown beyond infancy in North America. These observations should be borne in mind when evaluating the nutritional adequacy of diets of American children and adolescents.

The requirement of vitamin D in adult life is not known. The occurrence of deficiency states (though very rare) indicates that a small need exists,[1] but it is considered that the amounts required are so small that under normal circumstances they are met by the vitamin D content of the usual mixed diet and by exposure to sunlight. For persons working at night, and for nuns and others whose clothing or customs shield them from sunlight, the regular consumption of vitamin D-fortified milk is recommended.

The requirement for vitamin D during pregnancy and lactation also is not known. On the basis of the small amount of evidence,[7] a daily intake of 400 IU is recommended during pregnancy and lactation.

Toxicity

It has long been recognized that excessive amounts of vitamin D (of the order of 1,000 to 3,000 IU/kg/day) are potentially dangerous to children[14] and adults[15] and may lead to hypercalcemia and attendant

complications. It had first been thought that the margin of safety between the vitamin requirement and its toxic dosage was very great. However, relatively recently, circumstantial evidence derived from epidemiologic and metabolic studies of infantile hypercalcemia has tended to implicate vitamin D in the pathogenesis of both the mild and severe forms of this disease.[1,16-19] Vitamin D intakes implicated in hypercalcemia have usually been in the range of 2,000 to 3,000 IU/day, but sometimes the intake has been considerably less than this, and hypersensitivity to vitamin D has been postulated as an additional factor in affected individuals.[1,20] Although the relationship with vitamin D has not been completely proved, and recent estimates [20] place the incidence of infantile hypercalcemia at an extremely low figure, there is a justifiable basis for recommending that vitamin D intakes should not appreciably exceed a total of 400 IU/day during infancy.[1] There is no evidence that intakes of the order of 2,000 to 3,000 IU/day produce hypercalcemia beyond infancy. However, because the long-range effects of small excesses of vitamin D have not been extensively studied in vitamin D-sensitive individuals, the above recommendation for infants is also justified for older children and adults.

Considerations

The decline in the incidence of rickets in the United States in recent decades can largely be credited to the addition of vitamin D to fluid and evaporated milk. Few natural foods contain more than minute amounts of vitamin D. However, in the United States, a number of other foods, such as margarine, milk-flavorings, and certain breakfast cereals, have vitamin D added.[1] In evaluating the total vitamin D intake of the individual in terms of the RDA, the vitamin D content of the milk, of the vitamin supplement, and of all fortified foods must be taken into account. In North America, individuals of all ages consuming an ordinary diet may ingest an appreciable amount of vitamin D without taking a vitamin supplement, and in some individuals the recommended allowance may be considerably exceeded.[1,18] Calculation of individual intakes is often difficult. Vitamin D-addition practices vary from country to country. In the United States, the types of foodstuffs being fortified and the vitamin D concentrations of individual food items are continually being altered by the manufacturers. It is estimated that 85 percent of the fluid milk marketed in the United States has vitamin D added to a concentration of 450 IU/1,000 ml, and almost all brands of evaporated milk and commercial infant formulas

contain this concentration when reconstituted.[1] Thus, within a few weeks of birth, most formula-fed full-term babies will acquire the RDA of vitamin D from the formula, and additional vitamin D is not necessary. Human milk and unfortified cow's milk contain minimal amounts of vitamin D, and, at the present time, fortification of nonfat dry milk is not permitted in the United States. Rickets may occur in breast-fed infants and in those fed unfortified formulas[7]; hence, for these infants a daily vitamin supplement providing 400 IU of vitamin D is recommended. During childhood and adolescence, consumption of vitamin D-fortified milk will usually provide a large proportion of the individual's recommended allowance of vitamin D. Milk consumption tends to be less during adult life, but the vitamin D requirement is also much lower. During pregnancy and lactation, however, many women consume at least one quart of milk per day. If vitamin D-fortified milk is used, the RDA of this nutrient is ingested.

VITAMIN E (α-TOCOPHEROL)

Vitamin E is an essential nutrient in more than twenty vertebrate species, including man. The earliest evidence of deficiency differs with the species, but eventually the hematopoietic, muscular, vascular, and central-nervous systems are affected, as well as the reproductive system in many species of animals, but not in man. The exact biochemical mechanism whereby vitamin E functions in the body is still unknown.

For practical purposes, the tocopherols other than α (e.g., β-, γ-, and δ-), because of their relatively lower potency than the α-form, are disregarded in dietary calculations and evaluations. One international unit of vitamin E is 1 mg of synthetic *dl*-α-tocopherol acetate. The natural form, *d*-α-tocopherol acetate, has a potency of 1.36 IU/mg. The free alcohol, *dl*-α-tocopherol, has 1.1 IU, and *d*-α-tocopherol has 1.49 IU/mg.[1]

In 1949, it was discovered that the normal resistance of red blood cells to rupture by oxidizing agents is markedly reduced in vitamin E deficiency.[2] In vitamin E-depleted monkeys and in some children with kwashiorkor, not only increased hemolysis but also megaloblastic anemia were found, and administration of vitamin E induced a reticulocyte response.[3,4] Studies on the vitamin E requirement of infants established that the amount necessary to prevent hemolysis was within a range of 2 to 10 IU.[5-7] Because of negligible placental transfer, newborn animals, including human infants, have low tissue concen-

trations of vitamin E. Human milk is relatively rich in tocopherol content (2 to 5 IU of α-tocopherol per liter) and would meet the infant's requirement, whereas cows' milk is relatively low (only about 1/10 to 1/2 of the amount in human milk) in vitamin E content and would not be adequate.

In male subjects,[8,9] vitamin E deficiency developed in diets containing 25 percent of calories as fat and supplying about 3 IU of vitamin E daily. As the intake of fat and polyunsaturated fatty acids (PUFA) increased, the requirement for vitamin E increased. The adult needs about 10 IU or less when PUFA intake is low (less than 7 g daily) and about 30 IU when PUFA intake is high (over 35 g/day) and total fat consumption is at the level currently prevalent in the United States (about 40 percent of calories).[8-10]

The increase in vitamin E requirement with increased PUFA intake was also observed in a study of prematures in which a vitamin E-deficiency syndrome developed in those infants receiving formulas relatively high in PUFA content.[11]

Vitamin E requirement apparently is not related to body weight directly nor to calorie intake. It does appear to be related to body weight in kilograms to the three-quarter power ($kg^{0.75}$), sometimes designated as physiologic or metabolic size.[12] (See Appendix 2 for tabulation of body weight, $kg^{0.75}$.) Some support for this relationship is provided by a comparison of vitamin E requirement of 11 species of animals of widely different sizes in which the requirement was found to be related to body weight to the 0.73 power, not significantly different from the commonly used body weight to the 0.75 power.[13] Calculation of recommended allowances as IU = 1.25 × body weight in $kg^{0.75}$ provides the values shown in the table. The calculated allowance for infants, 3 to 6 IU of vitamin E, is in good agreement with the range of 2 to 10 IU established from clinical studies.[5]

The effects of pregnancy or lactation on the requirement for vitamin E have not been established.

Estimates of vitamin E content of diets representative of foods available for daily consumption show wide variation—from about 2 to 66 IU.[10,14] These estimates are made from chemical analyses of individual foods in which there is a wide variation in tocopherol content. The apparent absence of vitamin E deficiency in the general population suggests that the amount of vitamin E in foods is adequate.

Food processing and storage destroy some of the tocopherol content of most foods, and even deep-freeze storage does not completely prevent oxidative destruction of tocopherols. However, ordinary cooking, except deep-fat frying, does not reduce tocopherol content. In the usual

HARVEY M. ROSS, M. D.
9201 SUNSET BOULEVARD · LOS ANGELES 90069
(213) 276-2325

August 7, 1973

Bob Ullman, Esquire
Bass and Ullman
342 Madison Ave
New York, New York 10017

Dear Mr. Ullman:

In referrence to the recent F.D.A. ruling to require prescription for vitamin A above 10,000 units and vitamin D above 400 units, I would like to add my opinion that this ruling has no valid purpose. While it is true that there may be some toxicity from vitamin A and D in large dosages, one must take vitamin A in excess of 100,000 units for a period of time longer than 6 months before toxicity would be expected. I have in my case histories a record of an elderly woman who participated in a study done somewhere which involved taking 300,000 units of A for a long period of time and she was on this dosage for one year before she began to show some side effects of loss of hair. This side effect was quickly reversed when the vitamin was discontinued. In my opinion there is no logical justification for the recent F.D.A. proposal and it seems that this is but a first step towards the total harrassment of all of us who believe in nutrition as a way to maintain and obtain good health.

Very truly yours,

Harvey M. Ross, M.D.

HMR:Tera
Enclosures

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HARVEY M. ROSS, M.D.

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1960	Psychiatric Residency, New York State Psychiatric Institute
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August 7, 1973

Mr. Robert Ullman
Bass & Ullman
342 Madison Avenue
New York, New York 10017

Dear Mr. Ullman:

In all my 20 years of medical practice, I have not seen or heard of any case of poisoning from Vitamin A or Vitamin D. My patients have taken Vitamin A in excess of 10,000 I.U. per dosage and Vitamin D in excess of 400 I.U. per dosage daily without any toxic effects.

The FDA proposal requiring a doctor's prescription for oral preparations containing Vitamin A in excess of 10,000 I.U. per dosage unit and Vitamin D in excess of 400 I.U. per dosage unit is unreasonable and without any valid purpose.

Sincerely,

J. P. Hutchins, M.D.

J. P. Hutchins, M.D.
President

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National Clearinghouse for Poison Control Centers

Bulletin

April-June 1972

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service
Food and Drug Administration
Washington, D.C. 20204

VITAMIN INGESTIONS
BY GEORGE D. ARMSTRONG

Over the past several years, vitamins have been exceeded only by aspirin in the number of ingestions reported to the Clearinghouse. In direct contradiction to other most frequently ingested products such as aspirin, bleaches and pesticides which trended downward, vitamin ingestions as overdoses in children increased from 1.7% in 1965 to 5.1% in 1969. In 1970 and again in 1971, a slight drop to 4.9% and 4.8%, respectively, is probably of little real significance.

Public and medical knowledge of the relative safety of vitamins probably results in a laxity in reporting ingestions. Were this factor eliminated, vitamin ingestions might have trended upward.

Although the percentage of vitamin ingestions dropped slightly, the total number of reported ingestions for children increased to 4053 in 1971. This represents the greatest number of ingestions of any year thus far, and an increase of almost 18% when compared to 1970. (There was a 9% increase of all reports in children under 5). Symptoms were reported in 127 cases and 45 children were hospitalized.

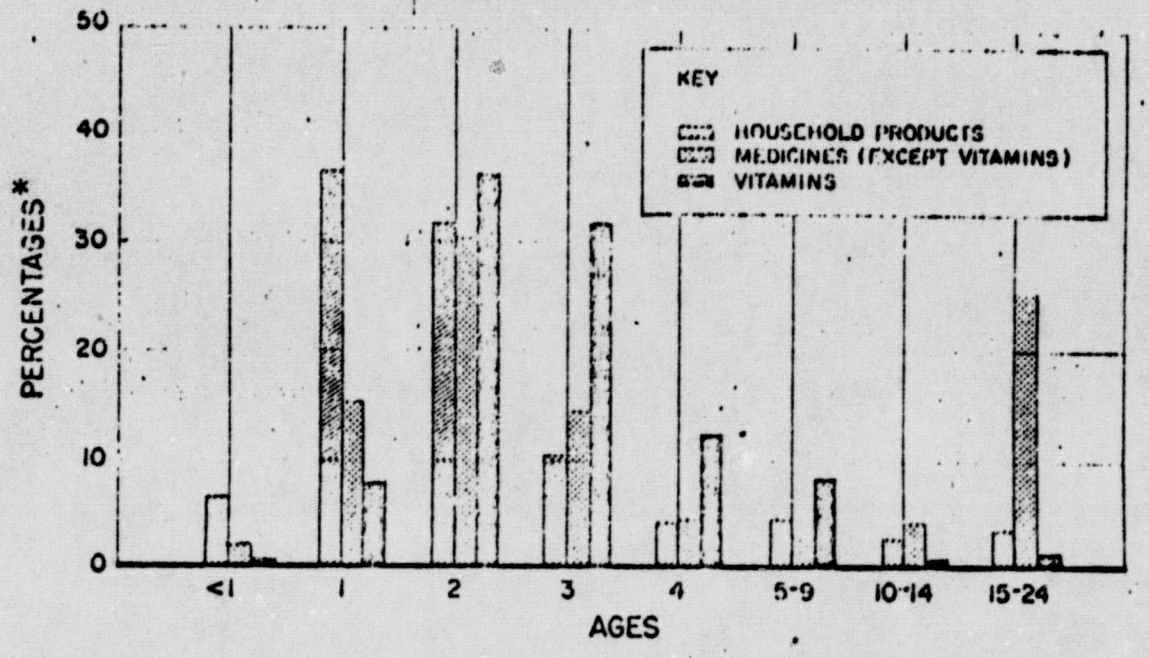
The causes of this constant rise in the number of ingestions are equivocal, at best, but surely some factors that influence the rise are availability, attractiveness, virtual universality of parental "overconcern" for childhood nutrition and increased numbers of total reports received from the Centers.

Vitamin manufacturers have been criticized for their not infrequent commercials depicting vitamins as "tasting good", "being friends", and other slogans which encourage confidence associations by children.

Vitamin poisonings in adults are usually associated with faddism. Ingestion of specific vitamins for "health kicks" and various ailments other than vitamin deficiencies has been surrounded by controversy. The use of vitamin E to prevent sterility, vitamin A to prevent infections, and, most recently,

(2)

COMPARISON OF RELATIVE AGE FREQUENCY OF 1971 INGESTION REPORTS OF VITAMINS, ALL OTHER MEDICINES AND HOUSEHOLD PRODUCTS



* THE PERCENTAGES WERE CALCULATED FROM THE TOTALS OF THE AGE GROUPS SHOWN.

vitamin C for the prevention and/or amelioration of colds has polarized both physicians and laymen alike into believers and non-believers. The object of this article, however, is not to examine these controversies, but to point out the fact that they do exist and that they might influence the number of ingestions reported to the Clearinghouse.

In the 1971 reported cases involving children that were treated, 908 of the 1030 total treated cases had no symptoms. Fifty-eight cases of nausea, vomiting, and/or abdominal pains were reported. Twelve children exhibited lethargy, two rashes, two pneumonias, two elevated temperatures, and one ataxia. Forty-five cases presented with other, unspecified symptoms. The cases reported as hospitalized (45) were not investigated for authenticity. No fatalities were reported. Of particular note is that over fifty percent of ingestions for all ages occurred in two and three year olds. Of the ingestions involving all age groups (4769), 4661 were considered accidental, 48 resulted from attempted self poisoning, and 60 were for unknown reasons. Four of the self poisonings were considered to be suicide attempts and 15 were gestures.

As illustrated by the graph, vitamin overdose is a childhood problem with abrupt decreases in the number of overdoses following the third year. Vitamin overdose follows the pattern

of all other medicines until the early teenage years. During the preteen years, the percentage of ingestions of all medicines rises upward from 0 years old to a peak at 2 years old, down to a plateau at 4 years old where the level remains fairly constant until the early teens. Vitamins follow a pattern that is similar but with certain distinguishing factors. The ascension to the peak at 2 years old is more abrupt but the decline is more gradual and continual without the leveling off that occurs with all other drugs. The third group shown on the graph is household products. As expected, the number of ingestions peaks early (at one year old) and declines as in all medicines to a fairly constant level at four years old.

Graph specifications:
formula -

$$\frac{\text{(number of ingestions of x category at y age) (100)}}{\text{number of ingestions of x category for ages 0-24 years}} = \%$$

for household products, n = 42308; vitamins, n = 4499; all other medicines, n = 53417

Multivitamins

As would be expected, multivitamins represented a large proportion of vitamin statistics. The quantities required to constitute an acute toxic dose of multivitamins are so massive as to virtually eliminate the possibility. Even multivitamins in combination with minerals or fluoride as a single ingestion should be of no more consequence than gastrointestinal irritation with or without purgation. However, chronic ingestion of large amounts could possibly cause hypervitaminoses A and/or D and fluorosis. A more probable cause of hypervitaminoses is the ingestion of therapeutic or high potency multivitamins or in single entity products of Vitamin A or D.

So called therapeutic and high potency vitamins often represent doubling of the standard formulation. From a toxicological standpoint, one needs to distinguish between the accepted meaning and the literal meaning of multivitamins. The general conception of multivitamins is that of a product that contains several B vitamins, vitamins A, C, and D, and possibly a small amount of iron. Literally, the definition of multivitamins is a product that consists of more than one vitamin. Using the literal definition, the potential for toxicity increases tremendously for some products and is essentially eliminated for others. For example, a product consisting of high concentrations of vitamins A and D has a much greater toxic potential than a product consisting entirely of the standard B vitamins (with the inference that the oral route is the method of administration). For the sake of clarity, the accepted definition of multivitamins is used throughout this

article.

Vitamin A

Acute vitamin A poisoning, following a single dose of several hundred thousand units, has been reported in infants. This would represent an extremely large quantity of multivitamins, but only 3 or 4 capsules of certain vitamin A preparations. Symptoms of acute intoxication in infants included increased intracranial pressure with bulging fontanel and vomiting. Discontinuance of the drug alleviated symptoms within three days.

Often studied, but still controversial, are the polar bear liver ingestion incidents. Most investigators agree that the rich vitamin A content of the liver was responsible for the toxic effects. However, agreement has not been reached as to whether toxicity was caused by a single ingestion or by chronic ingestions with acute onset of symptoms. In either case, the symptoms were acute in onset and developed in otherwise apparently healthy individuals within 24 hours postprandially. Symptoms included drowsiness, sluggishness, irritability, irresistable desire to sleep, severe headache, and vomiting, followed by peeling around the mouth within the first 24 hours. Later generalized peeling of the face and/or body occurs.

Interestingly, reports of "sloughing of skin from head to foot" following ingestion of polar bear liver date back to 1596. More recently, experiments involving single ingestions of polar bear liver had both symptomatic and asymptomatic results.

Chronic vitamin A intoxication, hypervitaminosis A, is characterized by disappearing eyebrows, dry rough skin, and cracked lips, followed by severe headache and generalized weakness. Premature closure of the epiphyses and arthralgia are common in children. Decalcification of bone, hemorrhage, and enlargement of the liver and spleen also occur. Hypervitaminosis A has, with one exception, been associated with intake of more than 100,000 units a day. Exactly how vitamin A exerts its toxic effects is not known.

Vitamin D

From an acute single ingestion standpoint, vitamin D is nontoxic. Toxicity problems arise only from large doses for long periods of time. Initially, vitamin D was thought to have a wide margin of safety between the recommended and toxic doses. Recently, however, the margin of safety was found to be much narrower than once thought for chronic use in high doses. The so-called sunshine vitamin, due to the conversion of precursors to the vitamin in the presence of sunshine or other irradiation, has been incorporated in many foods such as milk and butter to insure adequate amounts in the diet. Ingestion of vitamin D in

doses of 100,000 units or more daily in adults or 4000 units or more daily in children has resulted in hypervitaminosis D. Symptoms simulate hypercalcemia and consist of weakness, fatigue, lassitude, headache, nausea, vomiting, diarrhea, anorexia and pruritus. Impairment of renal function may be manifest as polydipsia, polyuria, nocturia and albuminuria. Metastatic calcification of the kidney and other organs may result in irreversible damage. Treatment consists of immediate withdrawal of the vitamin, a low calcium diet and a generous fluid intake along with acidification of the urine. Cortisol has been used to lower plasma calcium levels to normal.

Other Vitamins

In discussing vitamins other than A and D, the distinctions between side effects, adverse effects, and toxic effects is often evasive. In fact, certain undesirable effects have been reported by some sources as adverse effects and by others as toxic effects. Undesirable effects have been reported from Vitamins C and K and niacin. As vitamin K is rarely found around the home it will not be considered in this article. Vitamin C in megadoses has been reported to cause diarrhea and mild diuresis. In fact, some physicians have used vitamin C in large doses for its laxative effect. According to the AMA Drug Evaluations 1971, "There is no evidence that large doses are harmful". Niacin in large doses for long periods of time has been reported to cause hyperglycemia, jaundice, gastrointestinal irritation, and peptic ulcer. In therapeutic doses, peripheral vasodilation with resultant flushing and pruritus has occurred. Niacinamide, which exhibits the same activity as niacin except for vasodilation, has largely replaced niacin in vitamin preparations. Vitamin E and the other B complex vitamins are essentially non-toxic when given orally.

SUMMARY

Of the vitamins commonly found in the homes, only vitamin A possesses significant single-dose toxicity potential. Therefore, when a physician or poison control center receives a call concerning a vitamin ingestion he should attempt to decipher the ingredients of the preparations with particular note to vitamin A and iron, and their concentrations. If they are not present or are in subtoxic concentrations then giving the child milk should be sufficient placebo to appease the child's parents. If iron intoxication is imminent then the patient should be treated accordingly. Although single ingestion vitamin A poisonings are rare, they have occurred. If potentially toxic amounts have been ingested, treatment should consist of emesis or lavage followed by symptomatic treatment.

Acute symptoms from chronic ingestion of vitamins A and D should be treated as described earlier.

In conclusion, vitamin ingestions as overdoses usually follow a benign, asymptomatic course with unremarkable recovery following discontinuance of the drug. However, the possibility for toxic symptoms, debility and death should not be excluded, especially when high dose chronic intake of vitamins A and/or D are involved.

during the week. Isn't it true, Doctor, that the toxic effects of Vitamin D have been observed in adults receiving 100,000 units per day for several months?

A Yes.

Q Are you acquainted with the Merck Manual, 11th Edition?

A Yes.

Q If it appeared in that manual, would you accept it?

A The Merck Manual I think is probably true.

Q Now, we had children on Vitamin A. Now, as for adults, Hypervitaminosis A, isn't it true, Doctor, that this condition has been described only in patients receiving in excess of 100,000 units a day?

A That would be very plausible.

Q If that statement appeared once again in the Merck Manual, would you accept it?

A As probably correct, yes. Of course, in all of these, Mr. Pendergast, you have to consider the time, the length of time. So that when I say I would consider it, it would depend on how long. If you took, say, 50,000 for two or three years, that might give a worse effect than taking 500,000 for three weeks or a month.

So when I am very vague about this, it is because your questions do not give me amounts and time, duration. All of this must be taken into account. In a particular individual, there will be variations in different individuals, many variables.

tissue, and the lungs and kidney are 40 times as rich as muscle. Inasmuch as this vitamin is so important for growth it is interesting to find it in large quantities in milk and in the yolk of eggs. In fact, milk, eggs and green vegetables are the chief sources of this vitamin for man. Cod-liver oil has long held a position of importance in medicine because it contains large amounts of this vitamin in addition to the antirachitic factor (vitamin D). The livers of other fish than the cod contain much larger quantities of this vitamin than does the liver of that species. For example, the liver of the halibut may contain 100 times as much; in fact 1 per cent by weight of halibut-liver oil may be vitamin A. The cod, like other fish, gets its supply of vitamin indirectly from the algæ upon which the smaller fish and lower forms of marine life feed, and these small fish serving as food for the cod furnish it with the vitamin, which in turn is stored in the fat of the liver.

On account of its solubility in fats, vitamin A is stored in the animal body in larger amounts than are some of the other vitamins, so that no symptoms of deprivation are seen until this store has become exhausted. Young adult rats apparently can store sufficient to keep them alive for about 6 months. Probably 95 per cent of the vitamin is stored in the liver. The accumulation in the liver is lowest at birth and tends to increase with age. Milk, eggs, and other foods contain a mixture of vitamin and carotene, the proportions of each varying often according to species. For example, about two-thirds of the vitamin activity of Guernsey milk is due to carotene while Ayrshire milk owes about one-third of its activity to carotene, and in Jersey milk there are about equal quantities of vitamin and provitamin.

Absorption and Excretion

Vitamin A is absorbed well, reaching its maximum blood level in 3 to 5 hours after administration. The absorption of carotene is more variable and slower, reaching its maximum in 7 to 8 hours. Carotene dissolved in oils or given with a fat diet is utilized well, but when given with a low-fat diet its absorption is less satisfactory. It should not be given with liquid petrolatum as it is soluble in this vehicle and, therefore, will not be absorbed. In the presence of hypothyroidism, also, the body is unable to utilize carotene.

When large amounts of vitamin A are ingested, part is stored in the body while the remainder is destroyed, very little being found in the excreta.

Toxicology

Following the ingestion of excessive amounts of the vitamin (100,000 units or more daily for several months) toxic symptoms may ensue. These include anorexia, irritability, pruritus, alopecia, tenderness of the bones, hepatomegaly, and neurological disturbances suggestive of a brain tumor. Ocular changes include papilledema, paralysis of the extra-ocular muscles, diplopia and rarely, exophthalmos. The effects on the bone resemble those induced by parathyroid hormone but, unlike the hormone, vitamin A also affects the cartilage and causes periosteal proliferation of the bones. Acute vitamin A intoxication has occurred in arctic explorers after eating polar bear or bearded seal liver and in infants and children given excessive doses. Rapid recovery follows withdrawal of the vitamin.

oil, such as salmon, sardines, and herring, are rich natural sources of the vitamin. The yolk of eggs is also an excellent source, and it is not destroyed by boiling or by storage. Milk and butter do not contain much vitamin D unless the cows from which they are derived are fed irradiated foodstuffs. Living plant tissues such as leafy vegetables probably contain no vitamin D. Exposure to the sunlight serves as the principal method whereby the organism obtains its requirement for the essential vitamin. Persons who do not expose themselves to light (as among the Moslems who practice Purdah) are for this reason liable to suffer from osteomalacia, the form in which avitaminosis D affects the adult. Even where the diet is deficient in vitamin D, exposure to sunlight, as among the laborers of the Orient, prevents the appearance of the disorder.

Action

Vitamin D facilitates the absorption of calcium from the intestine and is essential for the normal deposition of mineral in the osteoid and cartilaginous matrix of bone. The mechanism of this action and the metabolism of vitamin D in the body are not established. Since vitamin D activates alkaline phosphatase, an enzyme concerned in bone metabolism, it has been suggested that the vitamin is concerned in the action of this enzyme.

Metabolic balance studies in the human indicate that vitamin D stimulates the intestinal absorption of calcium only in cases of rickets but not when given to normal subjects, except occasionally as a late and probably secondary phenomenon. The effects of vitamin D on the serum and urinary calcium are largely independent of each other. The increase in serum calcium is due to withdrawal of calcium from bone; the increase in serum phosphorus results in an elevated urinary excretion of phosphorus. Only in severe cases of refractory rickets does vitamin D in large doses increase tubular reabsorption of phosphorus. Some patients with sarcoidosis are hypersensitive to vitamin D and respond by an elevation in serum calcium. This hypersensitivity is antagonized by cortisone, the administration of which in sarcoidosis results in a decline of the elevated serum calcium to normal.

Toxicology

Excessive amounts of vitamin D lead to a condition of hypervitaminosis. With moderate overdosage there is a fall in the amount of calcium and phosphate in the intestinal contents and an overcalcification at the growing ends of bone. The latter condition is ascribed to the excessive calcium and phosphorus in the blood and the action of the phosphatase or calcifying enzyme. In severe poisoning with this vitamin the calcium and phosphate may be drawn from the bones in spite of the overcalcified epiphyses, and there may be a net loss of mineral salts in the bones. Abnormal deposition of calcium in the blood-vessels and soft tissues has also been described after the administration of excessive doses of certain artificially prepared concentrates containing vitamin D. More recent work indicates that the toxicity observed in earlier work was due to the presence of impurities in irradiated mixtures. There is a wide margin of safety in the use of purified preparations and entire safety in the use of natural preparations.

Therapeutic Use

Exposure to sunlight remains for the adult the chief means for avoiding avitaminosis D. The routine prophylactic administration of some form of vitamin D, as fish oil, viosterol, or calciferol, is advocated for children. Vitamin D is a specific for the cure of rickets and osteomalacia. The use of some vitamin D preparation is also advocated during pregnancy, since the demand for the vitamin is increased by gestation.

The recommended daily allowance of vitamin D is shown in Table 38 1. Premature infants require large doses (1,000 units). For the treatment of rickets and osteomalacia the administration of 1,500 units daily are advocated. In certain cases of "refractory" rickets in which the normal response to vitamin D therapy is not observed, massive doses may be required. However, when using doses greater than 20,000 units daily for infants or 50,000 units for a child, weekly determinations of the blood calcium level should be made since vitamin D in large doses may raise the blood calcium to toxic levels.

The use of dihydrotachysterol, a compound related to vitamin D_2, in hypoparathyroidism, has already been described in Chapter 34.

U.S.P. PREPARATIONS

ACTIVATED 7-DEHYDROCHOLESTEROL. Activated 5,7-Cholestadien-3β-ol, Cholecalciferol, Vitamin D_3, $C_{27}H_{44}O$, occurs as white, odorless crystals. It is insoluble in water. Usual dose – Daily, 10 mcg. (400 U.S.P. Vitamin D Units); in rickets, prophylactic, 10 mcg. (400 Units), and therapeutic, 125 mcg. (5000 Units); in hypocalcemic tetany, up to 5 mg. (200,000 Units).

CALCIFEROL, Ergocalciferol, Vitamin D_2, $C_{28}H_{44}O$, occurs as white, odorless crystals. It is insoluble in water; soluble in alcohol, in chloroform, in ether, and in fatty oils. Usual dose – Daily, 10 mcg. (400 U.S.P. Vitamin D Units); in rickets, prophylactic, 10 mcg. (400 Units), and therapeutic, 125 mcg. (5000 Units); in hypocalcemic tetany, up to 5 mg. (200,000 Units).

CALCIFEROL CAPSULES, as usually available, contain the following amounts of Calciferol: 1.25 mg. (50,000 U.S.P. Vitamin D Units). Category and dose *See* CALCIFEROL.

CALCIFEROL SOLUTION is a solution of calciferol in an edible vegetable oil or in polysorbate 80 or in propylene glycol. It contains, in each Gm., not less than 0.25 mg. (10,000 U.S.P. Vitamin D Units) of $C_{28}H_{44}O$. Category and dose *See* CALCIFEROL.

VITAMIN E

Evans and his co-workers found that when rats were fed on synthetic food mixtures with the proper mineral constituents added and vitamins A and B the animals would grow and appear to be perfectly normal, but sooner or later became sterile. The sterility is due to a deficiency in the diet of certain natural foods containing vitamin E, and can be cured by giving these foods or by giving concentrated extracts of the foods. In the male there are changes in the germ cells passing on in severe cases to loss of the seminiferous epithelium, while in the female there is death and resorption of the developing embryos. The growth of the embryos seems to be normal for a time, but about the eighth day there is retardation in development, and fetal deaths occur about the twelfth day, although there

A Vitamin D, excessive doses of D could be toxic; of K could be toxic.

Q Getting away now from the stipulated population group of infants, what amounts of what agents would be toxic?

A To an adult?

Q Yes. To and adult.

A Amounts in excess of 100,000 units of vitamin A per day could be toxic to an adult and produce nerve damage.

Q Over what period of time?

A That would depend on the body stores the individual started with at the beginning of the period of ingestion of a large dose.

Q Doctor, this 1968 publication of the recommended dietary allowances that you have at your left hand --

EXAMINER HARRIS: P-651.

MR. ULLMAN: Yes, sir.

BY MR. ULLMAN:

Q Is it not a fact that the 1968 RDA publication talks of manifestations of vitamin A toxicity in large doses of 20 to 30 times the RDA's, that is 100,000 to 500,000 units?

A That is why I said over 100,000.

Q Are you personally familiar with any recent reports of vitamin A toxicity in any reputable publication, say the Journal of the American Medical Association?

A There is a report in the American Journal of Medicine

nb-6

on nerve toxicity of vitamin A.

Q What was the toxic amount of vitamin A involved in that report?

A There were several cases reported. The amounts were in excess of 100,000 a day.

Q Are you familiar with the last report of vitamin A toxicity in the Journal of the American Medical Association?

A To which report do you refer?

Q Report in the Journal of the American Medical Association, August 28, 1967.

A Could you show me that reference, please?

EXAMINER HARRIS: Has it been previously identified, Mr. Ullman?

MR. ULLMAN: No, Your Honor. I will be glad to have it marked.

EXAMINER HARRIS: Journal of the American Medical Association, August 28, 1967. O-224-62 -- is it?

MR. ULLMAN: 55, sir.

EXAMINER HARRIS: 55.

(Exhibit No. O-224-55 was marked for identification.)

BY MR. ULLMAN:

Q Doctor, do you happen to be familiar with this report?

A I don't recall reading --

EXAMINER HARRIS: Excuse me, Doctor.

iron deficiency anemia in the patients at the Johns Hopkins Comprehensive Child Care Center?

A I believe they fall in the same category.

Q By that, you mean in the same general range, this 33 percent figure?

A The range, yes.

Q Turning to your answer 22, Doctor, you were there discussing supplemental levels, or therapeutic levels of vitamins. In the last sentence of that answer you mention "special toxicity problems with respect to the fat soluble vitamins, especially A and D, when ingested by the infant."

Would I be correct that the chronic toxic dose in the child age group one to three would be in the neighborhood of 100,000 International Units per day over a period of about six months?

A I don't think it would take six months. I think the dosage range is about right. But it would produce toxic manifestations in considerably less than six months.

Q Approximately what period of time?

A Several -- two or three months.

Q But the dosage range of about 100,000 units per day is essentially correct?

A Yes.

Q With respect to vitamin D, are you familiar with the American Academy of Pediatrics' recommendation or finding with

Q What do you mean by "essential"?

A By "essential" we mean the body can not synthesize these amino acids at a rate which will provide maximum growth and maximum health.

Q Does the same hold true as to the fatty acids?

A Linoleic acid has been accepted, plus linolenic acid, as the two that must be provided in the diet, because man and many other animals are unable to synthesize those two fatty acids.

Q Are there others scientists believe are needed in human nutrition?

A Not that I know of.

Q On page 2433, Doctor, you were discussing on lines 19 through 25 the maxima in the RDAs, and you were specific about the possibility of excessive intake of the fat-soluble vitamins. Those are vitamins A and D, are they not, Doctor?

A Primarily, yes.

Q Is it not true that hypervitaminosis A has been found generally in children in amounts of 50,000 to 500,000 units per day?

A In that general area, yes.

Q Do you recall the RDAs?

A Five thousand for Vitamin A, for adults.

Q So that hypervitaminosis condition is in the area of 10 to 100 times higher?

A. Approximately.

Q. Is it not true that hypervitaminosis D has been found to result generally from ingestion of 150,000 units or more a day?

A. In this case of hypercalcemia in children.

In Great Britain there is no valid information which would permit us to say that these children were getting a definite level of Vitamin D in their diet. So that as far as I am aware the implication has been made that in Great Britain the infants with hypercalcemia have gotten considerably lower than -- you said 500,000, was it?

Q. 150,000 units daily.

A. -- 150,000 daily. Yes. The implication has been that they have been getting considerably less than that. But I can not say what they have been getting.

MR. PENDERGAST: I would like to have marked for identification the "Pharmacological Basis of Therapeutics," by Goodman and Gilman.

EXAMINER HARRIS: Has that not been identified?

MR. PENDERGAST: Only various pages.

EXAMINER HARRIS: What pages do you want?

MR. PENDERGAST: Page 1691. I believe the latest edition is the Third Edition.

EXAMINER HARRIS: 0-228-94.

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(Exhibit 0-228-94, was marked for identification.)

BY MR. PENDERGAST:

Q Are you acquainted with this text which I just identified?

A Yes, I have used it.

Q Do you find it a reputable text?

A Yes, sir, some parts.

Q Are we going to find a part that is not?

A I am not sure.

Q I show you page 1692, the right-hand column entitled "Hypervitaminosis D," where it says: "As a rough approximation it may be stated that the continued ingestion of 150,000 units or more daily may result in poisoning."

Do you accept that as an accurate statement?

MR. ANDERSON: Objection. No contradiction.

EXAMINER HARRIS: Sustained.

MR. PENDERGAST: All right.

MR. ANDERSON: I wonder, sir, if we could set up a situation where prior to the reading of these comments into the transcript I could get a look at what is being proffered? I hate to leap up and interrupt counsel. But the offer is never made to me. Therefore, we have the material read into the record.

EXAMINER HARRIS: It might save time.

MR. ANDERSON: It might, sir.

EXAMINER HARRIS: I have on occasion had that done.

MR. ANDERSON: Yes, sir.

MR. PENDERGAST: If Mr. Anderson will just tell me what he wants, I will comply.

MR. ANDERSON: It is just that I hate to jump up and interrupt.

EXAMINER HARRIS: The next time you have an excerpt for contradiction purposes show it to Mr. Anderson before you read it.

MR. PENDERGAST: Yes, sir.

MR. KLEINFELD: Is this directed to all counsel?

EXAMINER HARRIS: It might save time.

MR. KLEINFELD: I prefer not to. It is improper. It gives Mr. Anderson a chance to make objections and speeches, and it is not appropriate.

EXAMINER HARRIS: Mr. Anderson is entitled to make objections.

MR. KLEINFELD: At the right time.

EXAMINER HARRIS: It should be before you read the excerpt into the record.

MR. KLEINFELD: Yes, sir. But he knows before I read the excerpt, or anybody reads the excerpts, whether there is a contradiction. I think it is most unfair to give Mr. Anderson the copy before I read something to the witness, or

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show it to him.

EXAMINER HARRIS: I will handle it at the proper time. Let opposing counsel show the excerpts to Mr. Anderson before they are read.

BY MR. PENDERGAST:

Q Is it not true that the possibility of excessive intakes of Vitamins A and D is a possibility only when you reach levels far higher than the RDAs?

A In the case of infants I am not ready to say "Yes" as an answer to this, because the evidence from England -- this which I have seen -- is still not complete enough to permit putting any ceiling below which toxicity did not develop in these children.

Q How about adults?

A Adults are much less susceptible, or appear to be, to toxicity from Vitamins A and D, than infants.

Q Would I be fair then in characterizing your answer to my question to be that for adults the answer is Yes?

A They can take these levels, somewhere in the neighborhood of 100 -- is it 150 that Goodman and Gilman listed? -- 150,000 international units of Vitamin D, over a short period of time, without showing too many sumptoms of toxicity.

Q On page 2445 of the transcript you were asked concerning a product containing egg calcium products. Egg

COMPOSITION OF FOODS, 100 GRAMS, EDIBLE PORTION

Item No.	Food and Description	Vitamin A Value Internat'l Units
11	Amarinth, raw	6,100
37	Apricots: Dehydrated, sulfured, nugget-type & Pieces: uncooked	14,100
39	Apricots: Dried, sulfured: uncooked	10,900
110	Meats, poultry, etc; canned Liver, strained	24,000
111	Liver & Bacon, strained	22,000
118	Vegetables, canned: Carrots	13,000
121	Spinach, creamed	5,000
392	Beet greens, common: Raw	6,100
393	Cooked, boiled, drained	5,100
619	Carrots: Raw	11,000
620	Cooked, boiled, drained	10,500
621	Carrots: Canned: Reg. Pack Solids and liquid	10,000
622	Drained solids	15,000
624	Carrots: Special dietary pack (low-sodium) Solids and liquid	10,000
625	Drained solids	15,000
627	Carrots: Dehydrated	100,000
639	Chard, Swiss: Raw	6,500
640	Cooked, boiled, drained	5,400
695	Chicken: Fryers (weight, ready to cook, with giblets, more than 1-3/4 lbs.) Giblet: Cooked, fried	5,760
758	Chives, raw	5,800

EXHIBIT "N"

Item No.	Food and Description	Vitamin A Value Internat'l Units
	Collards:	
	Raw:	
805	Leaves, without stems	9,300
806	Leaves, including stems	6,500
	Cooked, boiled, drained:	
807	Leaves without stems, cooked in small amount of water	7,800
808	large amount of water	7,800
809	Leaves, including stems, cooked in samll amt. of water	5,400
	Frozen:	
810	Not thawed	6,800
811	Cooked, boiled, drained	6,800
	Cress, garden:	
935	Raw	9,300
	Cooked, boiled, drained,	
936	Cooked in small amt. of water, short time	7,700
937	Cooked in large amt. of water, long time	7,000
	Dandelion greens:	
950	Raw	14,000
951	Cooked, boiled, drained	11,700
	Dock (curly or narrowleaf dock, broadleaf dock, and sheep sorrel):	
953	Raw	12,900
954	Cooked, boiled, drained	10,800
	Eggs:	
	Dried:	
982	Yolk	5,980
	Kale:	
	Raw:	
1153	Leaves, without stems, midribs	10,000
1154	Leaves, including stems	8,900
	Cooked, boiled, drained:	
1155	Leaves, without stems, midribs	8,300
1156	Leaves, including stems	7,400
	Frozen:	
1157	Not thawed	8,200
1158	Cooked, boiled, drained	8,200

Item No.	Food and Description	Vitamin A Value Internat'l Units
	Lambsquarters:	
1239	Raw	11,600
1240	Cooked, boiled, drained	9,700
	Liver:	
	Beef:	
1266	Raw	43,900 */
1267	Cooked, fried	53,400 "
	Calf:	
1268	Raw	22,500 "
1269	Cooked, fried	32,700 "
	Chicken, all classes:	
1270	Raw	12,100 "
1271	Cooked, simmered	12,300 "
	Hog:	
1273	Raw	10,900 "
1274	Cooked, fried	14,900 "
	Lamb:	
1275	Raw	50,500 "
1276	Cooked, broiled	74,500 "
	Turkey, all classes:	
1277	Raw	17,700 "
1278	Cooked, simmered	17,500 "
	Mustard greens:	
1366	Raw	7,000
1367	Cooked, broiled, drained	5,800
	Frozen:	
1368	Not thawed	6,000
1369	Cooked, boiled, drained	6,000
	Mustard spinach: (tendergreen)	
1370	Raw	9,900
1371	Cooked, boiled, drained	8,200
1472	Parsley(common garden (plain) and curled-leaf varieties, raw	8,500
	Peaches:	
	Dehydrated, sulfured, nugget-type and pieces:	
1485	Uncooked	(5,000)

*/ Values vary widely in all kinds of liver, ranging from about 100 I.U. to more than 100,000 I.U. per 100 grams.

Item No.	Food and Description	Vitamin A Value Internat'l Units
	Peas and Carrots, frozen:	
1534	Not thawed	9,300
1535	Cooked, boiled, drained	9,300
	Peppers, hot, chili:	
	Mature, red:	
	Raw:	
1540	Pods, including seeds	21,600
1541	Pods, excluding seeds	21,600
1542	Canned, chili sauce	9,590
	Dried:	
1543	Pods	77,000
1544	Chili Powder with added seasoning	65,000
	Pokeberry (poke) shoots:	
1647	Raw	8,700
	Cooked, boiled, drained	8,700
	Pumpkin:	
1832	Canned	6,400
	Sausage, cold cuts, & luncheon meats:	
1986	Braunschweiger	6,530
	Liverwurst:	
2003	Fresh	6,350
2004	Smoked	6,530
	Spinach:	
2169	Raw	8,100
2170	Cooked, boiled, drained	8,100
	Canned:	
	Regular pack:	
2171	Solids and liquid	5,500
2172	Drained solids	8,000
	Special dietary pack (low-sodium):	
2174	Solids and liquid	5,500
2175	Drained solids	8,000
	Frozen: Chopped:	
2177	Not thawed	7,900
2178	Cooked, boiled, drained	7,900
	Leaf:	
2179	Not thawed	8,100
2180	Cooked, boiled, drained	8,100
	Squash:	
	Butternut:	
2205	Raw	5,700 */
2206	Baked	6,400 "
2207	Boiled, mashed	5,400 "

*/ Value based on freshly harvested squash. The carotenoid content increases during storage, the amount of increase varying according to variety and conditions of storage. More information is needed on the relative contents of the individual carotenoids and their rates of increase under usual storage conditions before a suitable vitamin A value can be derived for the stored product.

Item No.	Food and Description	Vitamin A Value International Units	
	Swamp cabbage:		
2238	Raw	6,300	
2239	Cooked, boiled, drained	5,200	
	Sweet potatoes:		
	Raw:		
2246	All commercial varieties	8,800	
2247	Firm-fleshed */(Jersey types)	9,200	**/
2248	Soft-fleshed " (mainly Puerto Rico variety)	8,700	***/
	Cooked, all:		
2249	Baked in skin	8,100	
2250	Boiled in skin	7,900	
2251	Candied	6,300	
	Canned: Liquid pack, solids and liquid:		
2252	Regular pack in sirup	5,000	
2253	Special dietary pack, without added sugar & salt	5,000	
2254	Vacuum or solid pack	7,800	
	Dehydrated flakes:		
2255	Dry form	47,000	****/
2256	Prepared with water	12,000	

*/ Term refers to the flesh of the cooked product.

**/ Values for commercial varieties having deep-orange flesh average about 10,000 I.U. per 100 grams; light yellow, about 600 I.U.

***/ Values for commercail varieties range from 8,000 to more than 20,000 I.U. per 100 grams. Porto Rico, the main variety, has a value around 8,000 I.U.

****/ Value varies widely; it is related to variety of sweet-potato. Range in dehydrated form is 21,000 to 72,000 I.U. per 100 grams, and 5,000 to 18,000 I.U. in product prepared for serving.

em No.	Food and Description	Vitamin A Value Internat'l Units
	Tomato Juice:	
	Dehydrated (crystals):	
92	Dry form	13,100
	Turnip greens, leaves, including stems:	
54	Raw	7,600
	Cooked, boiled, drained	
	cooked in -	
55	small amount of water, short time	6,300
56	large amount of water, long time	5,700
	Frozen:	
58	Not thawed	6,900
59	cooked, boiled, drained	6,900
	Vegetables, mixed (carrots, corn, peas, green snap beans, lima beans), frozen:	
03	Not thawed	5,000
08	Vinespinach (basella), raw	8,000

DEFENDANT'S NOTICE OF MOTION TO DISMISS

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

(Filed September 10, 1973)

THE NATIONAL NUTRITIONAL FOODS ASSOCIATION AND SOLGAR CO., INC.,

Plaintiffs,

-v-

CASPER W. WEINBERGER, Secretary of Health, Education and Welfare and ALEXANDER M. SCHMIDT, Commissioner of Food and Drugs,

Defendants.

NOTICE OF MOTION

73 Civ. 3448 (MEF)

S I R S :

PLEASE TAKE NOTICE, that upon the pleadings and a certified copy of the record on file with this Court, and upon all prior proceedings had herein, the defendants will move before the Honorable Marvin E. Frankel of this Court on September 17, 1973 at the United States Courthouse, Foley Square, New York, New York, or as soon thereafter as counsel may be heard, for an order, pursuant to Rule 12(b) of the Federal Rules of Civil Procedure dismissing this action and for such other and further relief as the Court may deem to be just in the circumstances.

Dated: New York, New York
September 6, 1973

Yours, etc.,

PAUL J. CURRAN
United States Attorney for the
Southern District of New York
Attorney for Defendants

By: /s/ [redacted]
[redacted]
Assistant United States Attorney
Office and Post Office Address:
United States Courthouse
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New York, New York 10007
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TO: BASS & ULLMAN
Attorneys for Plaintiffs
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New York, New York 10017

REPLY AFFIDAVIT OF JOSEPH JOHN VITALE
UNITED STATES DISTRICT COURT (Filed September 12, 1973) 92a
SOUTHERN DISTRICT OF NEW YORK

THE NATIONAL NUTRITIONAL FOODS ASSOCIATION and SOLGAR CO., INC.,

Plaintiffs,

-against-

CASPER W. WEINBERGER, Secretary of Health, Education and Welfare, and ALEXANDER M. SCHMIDT, Commissioner of Food and Drugs,

Defendants.

Index No. 73 Civ. 3448

REPLY AFFIDAVIT

STATE OF NEW YORK)
) SS.:
COUNTY OF NEW YORK)

JOSEPH JOHN VITALE, being duly sworn, deposes and says:

I am Professor of Community Medicine and Professor of Pathology at the Boston University School of Medicine; Director, Nutrition Programs, Boston University Schools of Medicine; and Senior Research Pathologist at the Mallory Institute of Pathology in Boston; and Professor of Medicine and Nutrition, Facultad de Medicina, Universidad de Antioquia, Medellin, Colombia. Previously I held the position of Professor of Nutrition at Tufts University School of Medicine. In addition, I was an Associate in Nutrition and then an Assistant Professor of Nutrition at the Harvard School of Public Health. I have also been Professor of Nutrition in the School of Medicine and in the College of Agriculture of the University of Wisconsin. Also, for two years I was a Visiting Professor of Nutrition at the School of Medicine,

Universidad del Valle, Cali, Colombia. During this time I was Scientific Director of a Cooperative Program in Nutrition between the Department of Nutrition at Harvard and the School of Medicine in Colombia.

I have taught courses in nutrition for many years. These included a three-month elective in nutrition research and training at the Universidad de Antioquia. I have also participated in providing lectures in nutritional pathology, within the Department of Pathology, at Tufts and at Harvard Medical School and participate in the nutrition teaching program at the Harvard School of Public Health. Finally, I have taught nutrition and the pathophysiology of malnutrition to the graduate students of the Frances Stern Nutrition Center at the Tufts-New England Medical Center. I have also been affiliated with the Frances Stern Nutrition Center which includes a clinic where outpatients are seen by therapeutic nutritionists as well as physicians, and where the patients' total nutritional needs are met and they are instructed in dietary management. I am also called upon by physicians to consult on nutritional problems.

Annexed hereto is a copy of my curriculum vitae which includes over 50 scientific articles published by me in the areas of public health, clinical and basic nutrition.

I am constantly in touch with the medical and scientific literature in the field of nutrition and keep current in the area by constant reading of articles on the subject in leading medical and scientific journals.

On the basis of my scientific experience, including

research, clinical and teaching experience, and my study of the medical and scientific literature, I am led to the conclusion that the recent regulations published by the Food and Drug Administration requiring a prescription for Vitamins A and D at levels above 10,000 IU and 400 IU respectively have no scientific basis. In matter of fact there is no scientific evidence to even support any possible contention of toxicity at levels at three to five times the Recommended Daily Allowance for said vitamins.

The letters submitted by the Food and Drug Administration do not constitute scientific evidence contrary to the statements I have just made. For example, the letter of January 22, 1973 of Dr. George V. Mann (Exhibit D) contains no supportive references or rationale for his singular conclusion that all vitamins shall be put on a prescription requirement. If we were to adopt the philosophy propounded by Dr. Mann, as I understand it from his letter, it would necessarily follow that almost every over-the-counter product, except perhaps toothpaste or hair tonic, should be put on a prescription basis. It is this philosophy which has greater concern for me as a scientist and as a citizen than the regulations themselves which are presently before this Court. It is my opinion that a great deal of confusion is being created in this proceeding by discussing questions of toxicity and danger when in reality we are being presented with discussions of philosophy.

To the same effect, the other letters submitted by the FDA do not constitute scientific evidence of toxicity or danger

at any levels which are being discussed in the present regulation.

I am firmly in support of proper controls over products distributed to the American public. I also believe that there should be requirements for complete and accurate information about all products, in proper labeling, to both the professions and to the laity. I take exception, however, to the instant proposal for prescription requirements which I do not consider to be based upon scientific fact.

/s/
JOSEPH JOHN VITALE

Sworn to before me this
11th day of September, 1973.

ROBERT ULLMAN
Notary Public, State of New York
No. 30-4051700
Qualified in Nassau County
Commission Expires March 30, 1975

Curriculum Vitae

Name: Joseph John Vitale

Present Position:

a) Professor of ~~Nutrition~~ Pathology, Dept. Path.
Department of Preventive Medicine and Pathology
Professor of Community Medicine
Department of "

b) Director, Nutrition Programs
~~Boston~~ Tufts University School of Medicine

c) Senior Research Pathologist
Mallory Institute of Pathology
Boston City Hospital

d) Professor of Medicine and Nutrition
Facultad de Medicina
Universidad de Antioquia
Medellin, Colombia

Date & Place of Birth: December 14, 1924 - Boston, Massachusetts

Citizenship: U.S.A.

Marital Status: Married

Academic Training

Dates	Institution	Degrees
1947	Northeastern University (Biology)	B.S. (Boston)
1949	New York University (Medical School Physiology)	M.S. (N.Y.)
1951	Harvard School of Public Health (Nutrition)	Sc.D. (Boston)
	Harvard Medical School (Biochemistry)	
1966	Universidad de Antioquia	M.D. (Colombia)

Positions Held

Dates	Position	Institution or Agency
June - Sept. 1949	Toxicologist	Massachusetts Department of Public Safety
1951 - 1960	Research Assistant	Mallory Institute of Pathology
1951 - 1966	Research Associate in Nutrition	Harvard School of Public Health

Positions Held (cont.)

Dates	Position	Institution or Agency
1960 - 1962	Assistant Professor of Nutrition; Visiting Professor of Nutrition, Cali, Colombia	On leave - working on a Cooperative Program in Nutrition between the Department of Nutrition HSPH, and the School of Medicine, Universidad del Valle, Cali, Colombia
Feb., 1966 Oct., 1967	Professor of Nutrition Research Associate	College of Agriculture School of Medicine University of Wisconsin
1963 - Present	Co-Director, ~~Tufts~~ B.U. Antioquia Collaborative Nutrition Program	

Member of:

Sigma Xi (1954)
American Institute of Nutrition (1955)
British Nutrition Society (1956)
American Association for the Advancement of Science (1963)
American Society of Clinical Nutrition (1964)
American Public Health Association (1964)
Latin American Society of Nutrition (SLAN)

1959 Special consultant to Interdepartmental Committee on Nutrition for National Defense (ICNND) for Nutrition Survey in South Vietnam (3 months duration).

1959 Visiting lecturer, University of Tokyo Medical School

1959 Claude Bernard Professorship Award for the year 1959 (University of Montreal)

1960 Special consultant to ICNND for Nutrition Survey in Colombia

1960 - 1962 Scientific Director of Cali-Harvard Nutrition Project (Universidad del Valle, Facultad de Medicina, Cali, Colombia)

Invited Chairman, Scientific Session, Sixth International Congress of Nutrition. Edinburg, Scotland, 1963 (August 9 - 15)

Invited Speaker, Seventh International Congress of Tropical Medicine andMalaria. Rio de Janeiro, Brazil, 1963 (September 1-10)

Director of Summer Medical Student Program, 1963. Organized Summer Medical Research Program for seven second-year Harvard medical students in Cali (4) and Medellin (3), Faculties of Medicine, Colombia.

Director of Summer Medical Student Program, 1968. Summer Medical Research Program for three first-year and one fourth-year Tufts University School of Medicine medical students, in Medellin, Colombia, at the Universidad de Antioquia.

Co-Scientific Director, Medellin, Colombia-Harvard Nutrition Cooperative Program (1964-1966). As a result of these co-operative programs between the Department of Nutrition and the Faculties of Medicine; Dr. Vitale makes several trips a year to work in the Department of Medicine.

1966-1967 Co-Principal investigator (U.S.) of Medellin - Wisconsin collaborative Programs (now continuing from Boston).

1967 - Present Co-Director ~~Tufts~~ B.U.-Antioquia Nutrition Program. Dr. Hernan Velez, Co-Director from Antioquia Facultad de Medicina.

Latin American Associations:

The Cali-Harvard Cooperative Nutrition Program began on September 1, 1960. During the year preceding 1960, a number of conferences had been held between Dr. Stare, Chairman of the Department of Nutrition at the Harvard School of Public Health and the Dean of the School of Medicine in Cali, Colombia, to discuss the desirability of appreciably expanding a cooperative program in nutrition in Cali, Colombia. As a result of these conferences, it was decided that it would be mutually advantageous to develop a strong Department of Nutrition in the School of Medicine at Cali. With funds made available by the Rockefeller and Kellogg Foundations and with various personnel from the Department of Nutrition, Harvard University, efforts were directed toward increasing the activities of the new Department of Nutrition, officially organized on October 1, 1960. Dr. Joseph J. Vitale, Assistant Professor of Nutrition at Harvard, took a leave of absence and was in residence in Cali for approximately two years. The progress reports of the Cali-Harvard Nutrition Project are available.

During the Cali-Harvard Program basic clinical research and public health programs, a course in clinical nutrition, a metabolic unit, and pre-kwashiorkor clinics in communities were established. The new Department of Nutrition developed strong ties (collaborative programs) with several other departments including parasitology,

Surgery, Pathology, Pediatrics, Medicine and Preventive Medicine. Out of these programs came several publications published in the English medical literature.

Dr. Vitale has visited and given lectures at various institutions in Latin America. He speaks Spanish fluently.

The Cali-Harvard Program terminated in 1963 and Dr. Vitale was asked to develop a similar program at the Universidad de Antioquia, Facultad de Medicina, Medellin, Colombia. Since 1963, Dr. Vitale has been engaged in a cooperative nutritional program in collaboration with various members of the medical faculty in Medellin. Dr. Hernan Velez, Associate Professor of Medicine is the director of the nutrition program in Medellin. Several collaborative programs are now in existence. There is a four bed adult metabolic unit and an eight bed pediatric unit in Medellin at the University Hospital. This unit is for the study of nutritional diseases; e.g., anemias, malabsorption, kwashiorkor and others. In addition, the Nutrition Program maintains a study in a nearby village, Heliconia, where the effects of a food supplementation and a health service program on physical and mental development and on morbidity are being studied. Dr. Vitale spends approximately two months a year in Medellin. The Tufts-Medellin Nutrition Program also provides training in public health nutrition for Tufts and Antioquia medical students.

As in Cali, the Tufts-Antioquia Program has excellent rapport with most of the other medical school departments and enjoys excellent collaborative support from them.

Publications

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EXCERPTS FROM RECORD CERTIFIED BY DEFENDANT SCHMIDT
IN DISTRICT COURT

HOFFMANN-LA ROCHE INC.

NUTLEY • NEW JERSEY • 07110

February 9, 1973

Hearing Clerk
Department of Health
Education and Welfare
Room 6-88
5600 Fishers Lane
Rockville, Maryland 20852

Gentlemen:

Re: Proposed Statement of Policy - Vitamin A and Vitamin D - Federal Register, December 14, 1972

These comments are in connection with the above-referenced Notice of Proposed Rule Making which appeared in the Federal Register for Thursday, December 14, 1972 as corrected in the Federal Register of Thursday, January 4, 1973.

Hoffmann-La Roche Inc., a New Jersey corporation, is an "interested person" within the meaning of the above Notice, since it is a major manufacturer and supplier of bulk vitamins and is also a manufacturer and seller of both ethical and proprietary vitamin products.

1. GENERAL CONSIDERATIONS

In general, the thrust of the subject proposal is that limits should be set on

non-prescription levels of vitamins A and D because of toxicity questions. Our basic contention is that the questions raised by this proposal should be held pending a complete review by the appropriate OTC Drug Review Panel.

Our comments on the actual toxicity question are mainly directed to vitamin A, but it is our impression that vitamin D might be allowed on a non-prescription basis at a higher level than the suggested 400 I.U. without presenting significant toxicity problems.

While there are certain differences between vitamins A and D which give rise to a greater degree of concern with the latter, such as the fact that hypervitaminosis D in general provides symptoms which are more serious than those seen with Vitamin A, and the lower level of reversibility of hypervitaminosis D effects as opposed to those found with vitamin A, most likely comments will be received from other interested persons exploring the question of vitamin D toxicity in greater detail.

We recognize that both vitamin A and vitamin D when taken in excessive doses can cause toxicity problems, but the proposal largely ignores the issue of the actual levels which give rise to toxicity problems. While we share the desire to protect the public with regard to misuse of these vitamins, on the other hand,

any steps taken in this direction should be reasonable and scientifically sound based on the best available medical knowledge.

2. ACTION ON THIS PROPOSAL SHOULD AWAIT THE COMPLETION OF THE OTC DRUG REVIEW

The present proposal specifically states:

> "All vitamins are included among the over-the-counter drugs to be reviewed by an OTC Drug Advisory Review Panel...."

The present proposal is based on questions of toxicity only, and appears to be adopting an interim position until all issues in connection with these vitamins are fully aired by the appropriate OTC Drug Review Panel. We regard it as far more advisable to resolve all questions relating to specific vitamins at one time rather than to pursue them in a piecemeal fashion.

The adoption of the present proposal obviously would require reformulation and relabeling of a great many products. Should the OTC Panel ultimately reach different conclusions from those presented in this proposal, manufacturers would then be presented with these problems a second time. In the absence of some compelling necessity, this double burden should be avoided.

We no way suggest or imply that matters of convenience and expense to industry should predominate over questions of hazard to the public health. In the case of Vitamin A, at least, no such hazard has been shown requiring precipitate action.

Preparations containing Vitamin A at very high dosage levels have been marketed for many years. Now, with the OTC review nearly at hand, it is suddenly determined that a hazard exists requiring that action be taken. Having waited for twenty years or more it is difficult to see why we cannot wait another year or so for the completion of the OTC review. In fact, not only is there no greater hazard today than there was five years ago, ten years ago, fifteen years ago, or twenty years ago, but rather there is less hazard.

Based on a DESI notice published in the FEDERAL REGISTER of August 19, 1971, FDA notified industry by letter of January 12, 1972, that Vitamin A preparations containing 50,000 I.U. of Vitamin A would, among other things, have to be labeled for "prescription use only". Only a little more than a year ago Vitamin A preparations containing 50,000 I.U. or more were freely available to the general public, whereas today such preparations can only be obtained on a physician's prescription. As will be seen from the literature compilation to be discussed later, Vitamin A toxicity symptoms linked to dosages of less than 50,000 I.U. daily have been quite rare.

In view of the FDA action noted above, it is difficult to understand the statement in the preamble to the present proposal that: "At present vitamin A is available over the counter in dosage levels as high as 50,000 I.U. per dosage unit." If such products are being shipped in violation of the "prescription only" requirement, it would appear that FDA has ample authority to act without having to adopt the proposed policy statement.

It should be noted that, at least to the best of our knowledge, industry did not oppose FDA's action in limiting Vitamin A preparations containing 50,000 I.U. or more per dosage unit to prescription status only. We believe that this lack of opposition can be attributed to a recognition by industry that it was a reasonable limitation in the interest of the public health.

In summary, we contend that both the consumer and industry will be better served by delaying action on the present proposal and leaving the matter to a complete review by the OTC Drug Review Panel.

3. THE MEDICAL LITERATURE ON HYPERVITAMINOSIS A IN MAN DOES NOT SUPPORT THE PRESENT PROPOSAL

The Food Nutrition Board, National Research Council, National Academy of Sciences has concluded: "If large doses of vitamin A (20 to 30 times RDA) or of

carotene are ingested for long periods of time, manifestations of toxicity develop." Recommended Dietary Allowances (7th Ed. 1968), p. 23. It would appear that the conclusion of the Food Nutrition Board is generally supported in the literature with some exceptions.

In connection with this proposal, we have made a thorough review of the medical literature relating to hypervitaminosis A in man. The information from these articles has been summarized and compiled in tabular form. Attached hereto as Table 1 is a compilation of 72 articles on this subject. Also attached is a Table 1 Supplement which includes a compilation of 12 additional articles. All 44 articles included on the FDA bibliography referred to in the proposal are included in these compilations and are indicated by asterisks in column 1 of the tables.

We have analyzed the data in the articles included in Table 1 as to various factors involved in hypervitaminosis A. The articles in the Table 1 Supplement were not included in the analysis because the latter articles were not readily available and they were compiled at a later point. However, the additional articles cited in the Table 1 Supplement do not result in any significant alterations in the results of the analysis of the first 72 articles. It should be added that these articles rely almost entirely on subjective evaluation of data

obtained through patient histories. There is reason to believe, especially in cases of parental overdosing, that the actual daily dosage levels of vitamin A were underestimated.

a. Body Weight

With hypervitaminosis A the relationship between body weight and the number of units ingested daily appears to have some significance. Unfortunately it is rather difficult to make a completely accurate evaluation of this factor based on the references in the literature because in many cases the weight of the patient was not indicated. In order to get some feeling for this, however, we did look at those cases where weights were supplied and in cases where the weight was not given reference was made to a table of weights appearing in Textbook of Physiology and Biochemistry, Bell, Davidson, Scarborough (6th Ed.) pp. 1096-97.

The most significant finding in looking at the data in this way was that there were only a few cases where the daily dosage of vitamin A throughout the period of ingestion was less than 2,000 I.U. per kilogram of body weight. (Table 1, Nos. 15,23,24,30,31,38,40,52, and 53) Even here one of the cases (Table 1, No. 23) involved administration of vitamin A by I.M. injection. In another case, (Table 1, No.30) the history of the intake was in doubt and in two other cases (Table 1, Nos. 31 and 52) the amounts taken were not judged

to be toxic. It should be added that in most cases the amounts taken ranged up to levels far in excess of 2,000 I.U. per kilogram of body weight.

b. Age

A review of the literature compiled in Table 1 on the basis of age would tend to reinforce the hypothesis that body weight is a more important factor than age. Hypervitaminosis A symptoms have been noted in very young infants as well as in an individual over 65 years of age. A compilation of 110 cases in the medical literature relating hypervitaminosis A to age results in the following data:

HYPERVITAMINOSIS A BY AGE

No. Cases		Age of Subject
6		3 months or less
12		3 months - 1 year
16	57%	1 - 2 years
16		2 - 4 years
13		4 - 12 years
18		12 - 18 years
13		18 - 30 years
9	43%	30 - 50 years
7		over 50 years
110		

As can be seen there is a fairly even distribution among the various age groups noted, but there seems to be at least a preponderance of cases in children below 12 years of age.

c. Duration of Intake

Another important factor to be considered is the duration of the intake of excesses of vitamin A. Again it is difficult to establish clearly the total relationship among factors such as body weight, level of dosage and duration of intake, however, it should be noted that based on a study of 107 cases from the articles compiled in Table 1, 70% involved intake duration in excess of four months. Following is a summary of these 107 cases in terms of duration of the vitamin A intake:

HYPERVITAMINOSIS A - DURATION OF INTAKE

No. Cases		Duration of Intake
7		1 week or less
4	30%	1 week to 4 weeks
12		1 month to 4 months
10		4 months to 6 months
23		6 months to 1 year
26	70%	1 to 2 years
17		2 to 5 years
7		5 to 10 years
1		over 10 years

Based on the above data the general observation may be made when hypervitaminosis A has been encountered it has usually been associated with long-term ingestion.

d. Levels of Daily Ingestion

An analysis of 107 cases from the articles included in Table 1 reveals the following in terms of the daily intake involved.

HYPERVITAMINOSIS A - LEVEL OF DAILY INTAKE

No. Cases		Estimated Daily Intake, Orally
7		600,000 IU A or more
5		500,000 - 599,000 IU A
11	(78%)	400,000 - 499,000 IU A
12		300,000 - 399,000 IU A
24		200,000 - 299,000 IU A
24		100,000 - 199,000 IU A
16	(15%)	50,000 - 99,000 IU A
8	(7%)	Under 50,000 IU A
107		

As can readily be seen 78% of the cases involve estimated daily intakes of 100,000 IU or more. Only eight cases or 7% involve estimated daily intakes of less than 50,000 IU of vitamin A. Of the latter eight cases seven were infants and only one was an adult. A closer look at these cases is warranted.

Taking the cases of children first, a 29 month old child was given an estimated dosage of 37,500 IU of vitamin A for 510 days. The indication was that the vitamin A was administered in the form of a natural fish oil concentrate, probably oleum percomorph, which not only contained 60,000 IU of Vitamin A

per gram, but 8,500 IU of vitamin D per gram as well (Table 1, No. 3). A 12 month old child was given at least 25,000 I.U. of vitamin A daily for a period of 273 days (Table 1, No. 58). An infant weighing only 2.1 kg was given 12,000 IU of vitamin A daily in the form of multi-vitamin drops for a 7 day period (Table 1, No. 59). Four of these cases were treated together in the literature (Table 1, No. 68). They involved a 2 1/2 month old infant, a 3 1/2 month old infant and a 5 1/2 month old infant all of whom were given an estimated 22,500 IU daily for 60, 25 and 74 days respectively and a 4 month old infant who was given an estimated 17,500 IU of vitamin A for 98 days. In each of these cases it appears that liquid preparations were involved and that such preparations contained fairly substantial amounts of vitamin D as well as vitamin A.

The one case (Table 1, No. 30) involving hypervitaminosis A in an adult at an estimated dosage intake of less than 50,000 IU per day was that of a 62 year old woman. As stated by the author, because of the woman's neurotic state the patient history was in doubt and it is possible that the actual amount of vitamin A she was ingesting daily was underestimated. In this case it was indicated that the woman was taking high doses of vitamin A for a period of approximately eight years.

There are two cases reported in the literature involving adults who were ingesting an estimated 50,000 IU of vitamin A daily. The first of these (Table 1, No. 31)

involved a 79 year old man who had been taking vitamin A at a level of 50,000 IU daily for 17 years. While his liver did have a high vitamin A content there were no obvious signs or symptoms of vitamin A toxicity. The second case (Table 1, No. 53) involved a 54 year old man who had been ingesting 50,000 IU of vitamin A daily for approximately 3 years. This man was a house painter and it is not entirely clear that his symptoms were all related to vitamin A, since, because of his occupation, there was exposure to fumes from paint and solvents.

e. Types of Preparations and Reasons for Excessive Ingestion

Looking at the literature compiled in Table 1 as it relates to children, there are 60 cases. It is interesting to note that of these cases 17 involved overdoses with oleum percomorph a fish oil preparation which contained 60,000 IU of vitamin A and 8,500 IU of vitamin D per gram. Seven other cases involved oleum percomorph together with other products. Most of the cases reported on children involved liquid preparations and in many of them vitamin D was involved as well. Thirty-eight of the sixty cases were caused by parental over-dosing, six were caused by physicians prescriptions followed by parental over-dosing, and the remaining 16 cases were caused by physicians recommendations and/or treatment procedures.

There were 47 cases reported in the literature tabulated in Table 1 on adults. In 27 of those cases the preparation used was not reported, in 16 cases the product involved was a 50,000 IU preparation, in two cases emulsions were involved, in one case 25,000 IU tablets were taken, and in one case vitamin A was given by injection.

An analysis of these cases indicates that in 20 of them there was an initial prescription by a physician followed by self-medication, in 14 cases prescription or treatment by a physician was involved, and only 13 of the cases were entirely based on self-medication.

f. Miscellaneous Observations

There are two further points to be noted. The literature review fails to reveal any instances of mortality resulting from excessive consumption of commercial vitamin A preparations. Secondly, the reports in the medical literature do not support a finding that there has been a significant increase in the number of medical reports on hypervitaminosis A in man in recent years.

HYPERVITAMINOSIS A MEDICAL REPORTS BY YEAR *

1939 - 1	1955 - 3	1965 - 6
1944 - 1	1956 - 3	1966 - 3
1947 - 1	1958 - 2	1967 - 2
1948 - 2	1960 - 2	1968 - 3
1950 - 6	1961 - 4	1969 - 2
1951 - 7	1962 - 1	1970 - 6
1952 - 7	1963 - 2	1971 - 4
1953 - 4	1964 - 3	1972 - 6
1954 - 3		

* 84 medical literature references from Table 1 and Table 1 Supplement, including some general review articles which do not report new cases.

g. Conclusion

The present FDA proposal starts with the premise:

> "Large doses of vitamin A ... ingested over long periods of time can cause adverse effects, some of which are serious."

There is general agreement as to the truth of that statement and the data from the medical literature would confirm this. Other than the arbitrary selection of 10,000 IU of vitamin A, as the limit for non-prescription status, however, the proposal nowhere attempts to answer the question of the level of vitamin A which can actually cause problems. An analysis of the data would tend to support the action already taken by FDA in placing vitamin A dosage forms containing 50,000 IU or more per dosage unit on prescription only. There is certainly nothing in the literature which would support a limit of 10,000 IU of vitamin A per dosage unit in adults. While the data tend to support a lower limit in children's preparations than with adult preparations, with children it is liquid preparations which are generally implicated and this proposal offers little if anything, which would curtail misuse of such preparations.

4. THE ARTICLES IN THE FDA BIBLIOGRAPHY RELATING TO VITAMIN A STUDIES IN ANIMALS DO NOT SUPPORT THE PRESENT ACTION

A review of a number of the articles included on the FDA's list of articles pertinent to vitamin A toxicity studies in animals reveals little, if any, support for the

position taken in this proposal. Attempts at extrapolation of data from studies in rats and other animals to humans is tenuous at best and is not warranted in connection with this proposal.

Many of the articles refer to problems caused by vitamin A deficiencies rather than simply those caused by excesses of vitamin A. See "Fetal Death and Maldevelopment Resulting From Maternal Vitamin A Deficiency in the Rat," Proc. Soc. Exp. Biol. & Med. 72: 687 (Dec. 1949); "Excessive Vitamin A and Congenital Abnormalities," J.A.M.A. 153: 1176 (Nov. 28, 1953); "Disturbance of Embryonic Development by Maternal Vitamin Deficiencies," J. Cell. Comp. Physiol. 43: 208 (May 1954); "Vitamins and Hormones," 18: 552-554 (1960); "Effect of Vitamin A Deficiency or Excess on the Oxidative Phosphorylation by Rat Liver Mitochondria," J. Biol. Chem. 241(5): 1229-1232 (Mar. 10, 1966); and Giroud, A., Fed. Proc. 27(1): 172-3 (Jan, Feb, 1968).

Other articles dealing with excessive vitamin A as the cause of congenital abnormalities involve administration of very large amounts of vitamin A. For example, 35,000 I.U. daily administered via stomach tube to rats, "Excessive Intake of Vitamin A as a Cause of Congenital Anomalies in the Rat," Science 117: 535-536 (May 15, 1953); 75,000 to 150,000 I.U. on the ninth, tenth or eleventh

day of pregnancy in rats, "Congenital Hypervitaminosis A," Nutrition Reviews 17(9): 276-277 (Sept. 1959); 15,000 I.U. by intraperitoneal injection in mice, "Malformations of the Mouse Fetus Caused by Hypervitaminosis A...," Arch. Env. H. 10: 732-41 (May 1965); 50,000 to 125,000 I.U./kg. of body weight in beagles, "Teratogenicity of Vitamin A in the Canine," Fed. Proc. 26: 486 (Mar-Apr 1967); 120,000 I.U. or 600,000 I.U. of vitamin A before malformed rat fetuses occurred, "Problem of Embryotoxicity of Vitamin A," Dtsch. Tierarztl. Wschr. 78: 294-6 (May 15, 1971) (Ger.).

These are representative examples from the FDA's list of articles on vitamin A studies in animals. The animal data in these articles is not in accordance with human experience. To duplicate in humans the doses given to animals in these studies on a kilogram of body weight basis, would require truly massive doses many times in excess of the 10,000 I.U. limitation in the present proposal. In addition, such factors as differences in metabolism and gestation periods cannot be ignored. While these articles may be interesting scientifically, they do not appear to have any bearing on the present issues, especially since there are a number of articles previously discussed relating to vitamin A experience in humans.

5. IF ACTION ON THE PROPOSAL IS NOT DELAYED PENDING THE OTC DRUG REVIEW THE VITAMIN A LIMIT FOR ADULTS SHOULD BE RAISED TO 25,000 I.U.

While the best course would be to delay action on the present proposal until a complete review is made by the appropriate OTC Drug Panel, if the decision is

to act sooner, the proposed 10,000 I.U. limit on vitamin A is too low for adults. As shown in our review of the literature, symptoms of vitamin A toxicity have rarely been implicated in cases where persons were ingesting less than 50,000 I.U. per day and in most cases the levels have been substantially higher.

It is recognized that children are affected at lower dosage levels than adults, probably because of lower body weight. Accordingly, if action is to be taken on the present proposal, we suggest that the 10,000 I.U. limitation be retained in preparations designed for young children, but contend that the limit for adult preparations should be raised to 25,000 I.U.

In both cases, these levels would not only be safe in themselves for the subject groups, but also would provide a wide margin of safety. We would consider these suggested limits to be realistic based on the substantial body of medical knowledge reported in the literature in connection with vitamin A toxicity. These levels would also maintain in each group upper level limits of approximately the same ratio in terms of multiples of the RDAs. If necessary, adult preparations containing more than 10,000 I.U. up to and including 25,000 I.U. of vitamin A could be appropriately labeled to indicate that their use is restricted to "Adults only" and other appropriate precautions could also be included.

We must continue to recognize the inherent right of the American people to self-medicate where this can be done safely. The approach suggested above

would accomplish this by providing safe dosage levels to persons who desire to take higher levels of vitamin A without forcing them either to take multiple doses of lower dosage forms or having to visit physicians in order to obtain prescriptions. If further safeguards are considered necessary to protect against accidental ingestion by children, the possibility of using safety closures could be considered.

6. THE PROPOSAL COULD HAVE A NEGATIVE NUTRITIONAL EFFECT

The ten-state nutrition survey conducted during the 1968-1970 period by the Department of Health, Education, and Welfare revealed a high incidence of low vitamin A values among important segments of the United States population. See for example "Highlights from the Ten-State Nutrition Survey," Nutrition Today, July/August 1972. In most cases the nutritional needs of the subject groups would be met by ingestion of RDA levels of vitamin A and we do not suggest that most individuals would need daily levels of vitamin A in excess of RDA's in order to meet their nutritional requirements.

We do suggest that a great many people are uneasy in matters of health, especially where quesitons of toxicity are raised. In view of the prestige of the FDA among consumers, wide-spread publicity to the effect that FDA considers relatively low levels of vitamin A toxic, creates the possibility that at least some consumers

would overreact to such announcements and deliberately avoid ingesting any vitamin A. Even such a widely-used food as margarine is specifically labeled to contain 15,000 I.U. of vitamin A per pound. Thus, problems of vitamin A deficiency in the population could become more prevalent.

To avoid creating misinterpretation and undue apprehension in connection with vitamin A, any limitations imposed because of questions of toxicity should not be set at unreasonably low levels. Any limitations must be realistic in light of actual levels which do cause toxicity problems, while maintaining a reasonable margin of safety.

7. PROMOTION OF HIGH LEVELS OF VITAMINS A AND D

Part of the rationale for the proposed Statement of Policy as expressed in the subject notice is "that there is widespread promotion to the laity of excessive quantities of these vitamins for prophylaxis and treatment of a variety of diseases and disorders." We submit that to the extent distributors of vitamins engage in improper promotional activities there is adequate statutory and regulatory authority in the federal agencies having jurisdiciton to curtail such activities. Also mentioned is the fact that high doses of vitamin A have been recommended "in the lay press, on radio, and on television." To the extent that recommendations are made by those claiming expertise in nutrition who are not directly engaged

in the distribution of vitamins, such recommendations, where improper, should be countered by expanded efforts on the part of FDA to educate the consumer. Reputable manufacturers and distributors of vitamin products should not be held accountable for statements of others over whom they have no control and such situations should not serve as a rationale for new regulations. Such a regulatory philosophy would place reputable manufacturers in all fields at the mercy of commentators recommending misuse of their products.

The proposed policy statement would do little to eliminate such problems as may exist, since it will not eliminate unfounded nutritional recommendations "in the lay press, on the radio, and on television". Those who wish to accept such advice will simply take multiple doses of lower dosage forms or will seek prescriptions from physicians.

8. IF THE PROPOSED ACTION IS NOT DELAYED PENDING THE OTC DRUG REVIEW THE TIME ALLOWED FOR COMPLIANCE IS INADEQUATE

Under the present proposal only sixty (60) days are allowed after final promulgation, beyond which time noncomplying products could not be labeled or dispensed without being subject to regulatory proceedings. If action on this proposal is not delayed to allow a complete OTC Drug Panel Review, this time

period is far too short. It would not only result in severe economic loss to those having substantial inventories of vitamin A products in amounts greater than 10,000 I.U., but would also be difficult to meet in terms of reformulation and relabeling.

No time period would be too short if there were a genuine hazard to the public health, but, as pointed out elsewhere in these comments, no such hazard presently exists, especially in view of action already taken by FDA limiting dosage forms of vitamin A to "prescription only" status at the 50,000 I.U. level.

CONCLUSION

The present proposal should be held or withdrawn pending the outcome of the OTC review. The medical literature on vitamin A does not support a finding of hazard to the public health requiring action at this time, especially in view of the fact that products containing 50,000 I.U. or more have already been limited to prescription status.

If action is not stayed until the completion of the OTC review, the proposed non-prescription limit of 10,000 I.U. of vitamin A per dosage unit should

be retained only for preparations intended for children and for adult preparations the non-prescription limit should be 25,000 I.U. of vitamin A per dosage unit. Such limits would not only provide dosage forms which are safe in themselves for the indicated age categories, but would, in each case, also provide a wide margin of safety. In any event, a longer period of time should be allowed to effect any changes imposed.

Respectfully submitted,

HOFFMANN-LA ROCHE INC.

By E. B. Anderson
Vice President

Submitted in Quintuplicate
Certified Mail, R.R.R.

Table I

HYPERVITAMINOSIS A in MAN

Author(s) and Reference	Form of Product	Mode of Administration	Estimated Dosage	Duration	Toxicity (salient symptoms)	Cause, Origin or Reason for Toxicity	No. of Pts.	Age	Sex
1. H.W. Josephs, ☆ Amer. J. Dis. Child. 67:33-43, 1944	natural vitamin A halibut liver oil	orally	@ 240,000 U.S.P. units daily on occasion drank oil from bottle in undetermined amounts mother's statement	@ 2 yrs, 9 mos	hepatomegaly, splenomegaly, hypoplastic anemia, leukopenia, increased serum vitamin A, increased serum lipids, advanced skeletal development, clubbing of fingers, sparse, coarse hair, abnormal appetite for halibut liver oil	parental overdosing and accidental consumption, probably also received vitamin D from oil	1	3 yrs	M
2. J.A. Toomey & ☆ R.A. Morissette, Amer. J. Dis. Child. 73:473-480, April, 1947	natural vitamin A oleum percomorph	orally	@ 250,000 U.S.P. units daily — 500,000 U.S.P. units daily one or two teaspoons full daily mother's statement	@ 20 mos on lower dose and @ 3 mos on higher dose	hepatomegaly, increased serum vitamin A, increased serum lipids, bone abnormalities, increased serum phosphatase, low serum proteins, sparse, coarse hair, avid appetite for butter, pain and localized periosteal swellings	parental overdosing and accidental consumption, child was also given vitamin D (35,000-70,000 units) daily. Abnormally fond of butter	1	23 mos	M
3. B.H. Berrey, Pediatrics 6: 78-85, 1950	natural vitamin A probably oleum percomorph	orally	@ 37,500 I.U. daily 30 drops of natural fish oil concentrate daily mother's statement	@ 1 yr, 5 mos	postinfantile hyperostosis with subdural hematoma, hyperirritability, photophobia, fatigue, fever, anemia with leukocytosis, external thickenings of the corticallis of the bones	incorrect dose was given, child also received vitamin D (5,355 I.U. daily)	1	29 mos	F

Table I

4. J. Caffey, Pediatrics 5:672-688, 1950	natural vitamin A oleum percomorph or Drisdol + A or Navitol	orally	@ 100,000 - 600,000 I.U. daily mother's or father's statements	@ 6 mos - 17 mos	infantile cortical hyperostosis, increased serum vitamin A	parental overdosing, gave oleum percomorph instead of cod liver oil. Three children also received vitamin D (20,000-40,000 units daily)	7	12-37 mos	5 M, 2 F
5. C.T. Pried & M.J.H. Grand, Amer. J. Dis. Child. 79:475-486, March, 1950	natural vitamin A oleum percomorph	orally	@ 400,000 - 500,000 I.U. daily mother's statement	@ many months-over 1 yr	infantile cortical hyperostosis, greatly increased serum vitamin A also received vitamin D from oil	parental overdosing and accidental consumption, gave oleum percomorph instead of cod liver oil. One child ate excessive amounts of butter	2	16 mos 2 yrs	M
6. T.C. Wyatt, C.A. Carabello & M.E. Fletcher, JAMA 144:304-305, Sept. 23, 1950	natural vitamin A oleum percomorph	orally	@ 400,000 - 500,000 I.U. daily mother's statement	@ 2 yrs	anorexia, tenderness of extremities, low grade fever, generalized pruritus, weakness, pronounced irritability, pale skin, unsteady gait, x-ray changes of long bones, high serum vitamin A, upper respiratory infection	parental overdosing in the form of oleum percomorph, child was also given vitamin D (60,000 - 70,000 units daily)	1	3 yrs	F
7. J.M. Arena, P. Sarazen, Jr., & G.J. Baylin, Pediatrics 8:788-794, 1951	vitamin A oleum percomorph + ABDEC drops	orally	@ 80,000 - 82,500 U.S.P. units daily mother's statement	@ 2-1/2 mos	anorexia, hyperirritability, craniotabes, high serum vitamin A	physician's prescription, child was also given vitamin D (11,000-11,500 U.S.P. units daily)	1	6-1/2 mos	F

Table I

8. G. Bair, JAMA 146:1573-1574, 1951	vitamin A oleum percomorph	orally	@ 240,000 units grandmother's statement	@ 3 mos	pruritus, irritability, pain, swelling of bones, high serum vitamin A, cranial hyperostosis	grandmother overdosed child. The child also showed an avid appetite for dairy products (butter, milk, cheese), also ate tomatoes and sweet potatoes	1	28 mos	M
9. D. Gribetz, S.H. Silverman & A.E. Sobel, Pediatrics 7: 372-385, 1951	vitamin A oleum percomorph or Infadol	orally	@ 100,000 + U.S.P. units daily 240,000 units daily history by parents	@ 1-1/2 yr @ 7 mos	irritability, lip fissures, sparse, coarse hair, pain in extremities, high serum vitamin A, thickening of bones (cortical hyperostosis), elevated serum alkaline phosphatase	incorrect doses, were given. One child was also given vitamin D (20,000 U.S.P. units daily)	2	17 mos 2-1/2 yrs	1F 1M
10. I.E. Rineberg & R.J. Gross, JAMA 146:1222-1225, July 28, 1951	vitamin A Navitol	orally	@ 185,000 units daily mother's statement	@ 9 mos	infantile cortical hyperostosis, pain in limbs, frequent nose bleeds, upper respiratory infection	parental overdosing. The child also was given vitamin D (37,500 units daily)	1	33 mos	F
11. M.B. Sulzberger & M.P. Lazar, JAMA 146:788-793, June 30, 1951	vitamin A capsules of 50,000 IU	orally	@ 600,000 units daily and 1,000,000 - 2,000,000 on special occasions patient's statement-advised by radio nutrition commentator"	@ 18 mos	tenderness of various bones, slight bilateral exophthalmos, warm and dry skin, sparse, coarse hair, chloasma or Riehl's melanosis-like pigmentation, menstrual changes, pruritus, slight fissuring of nasal apertures and corners of mouth, acneform lesions on face, nails were soft and brittle, onychorrhexis, absence of radiologic changes of the bones	self medication	1	44 yrs	F

Table I

12. S.E. Goldzier, II, J.C. Pisacano & A.M. Wald, J. Pediat. 41: 198-201, 1952 *	natural vitamin A oleum percomorph	orally	@ 150,000 units daily for 4 mos and 300,000 units daily for 2 months mother's statement	@ 6 mos	hyperirritability, dry, coarse skin, thickening of extremities, hepatomegaly, high serum vitamin A, cortical hyperostosis, tenderness of bones	parental overdosing. Child was also given vitamin D (21,600-43,200 units daily)	1	24 mos	F
13. J.P. Naz & W.H. Edwards, New Engl. J. Med. 246:87-89, 1952	vitamin A oleum percomorph	orally	@ 220,000 units daily mother's statement	@ 8-1/2 mos	hyperirritability, anorexia, constipation, pruritus, sparse hair, palpable indurated swelling of head, lips dry and cracked, tenderness and brawny thickening of forearms, liver 2-1/2 finger breadths below right costal margin	parental overdosing. Child was also given vitamin D (31,680 units daily)	1	9 mos	F
14. G.C. Reyersbach, J. Hanelin & R.J. Joplin, New Engl. J. Med. 246:978-980, 1952	vitamin A oleum percomorph	orally	@ 240,000 units daily physician's recommendation	@ 1 yr	anorexia, irritability, pruritic skin rash, subcutaneous tender swelling, pain of the extremities, cracked dry lips, sparse, coarse hair, cortical hyperostoses, and a high vitamin A serum level	physician's prescription. Child also had an avid craving for butter	1	3 yrs	F
15. E. Bifulco, New Engl. J. Med. 248:690-692, 1953 *	vitamin A unreported source	orally	@ 100,000 I.U. daily as revealed by patient's history	@ 4 yrs	insomnia, coarse hair, loss of hair, pain in joints, exophthalmos, weakness, loss of weight, anorexia, pigmentation of forehead, bleeding from mucous membranes	physician's prescription	1	52 yrs	F
16. A.G. Knudson, Jr., & P.E. Rothman, Amer. J. Dis. Child. 85:316-334, 1953 (cite a case of Dr. Mary Mulloy)	natural vitamin A oleum percomorph	orally	@ 62,500 units daily mother's statement	@ 3 wks	tremors in extremities, bulging fontanelle, liver edge could be felt 3 cm below costal margin, high serum vitamin A	parental overdosing. Child was also given vitamin D (25,500 units daily)	1	7 wks	F

Table I

17. C.W. Shaw & J.Z. Niccoli, Ann. Internal. Med. * 39:131-134, 1953	vitamin A capsules of 50,000 or 25,000 IU	orally	@ 200,000 - 275,000 I.U. daily patient's comment - took capsules in lieu of a meal"	@ 2 mos	marked asthenia, 10 lb. weight loss, anorexia, polydipsia, polyuria, a skin rash, excessive hair loss over entire body, soreness and fissuring of lips, pain in shoulder joints, ribs, tibia and ankles, high serum vitamin A	self medication	1	25 yrs	M
18. A. Gerber, A.P. Raab & A.E. Sobel, * Amer. J. Med. 16: 729-745, 1954	vitamin A vitamin A only, preparation unreported	orally	@ over 500,000 units daily taken with hospital staff knowledge for a skin condition	over 8 yrs	severe headaches, visual disturbances, bone pains, pruritus, fissuring and soreness of mouth, alopecia, pigmentation of skin	self medication blood level 2000 mcg/100 ml highest ever recorded	1	28 yrs	F
19. R.A. Elliott, Jr. & R.L. Dryer, * JAMA 161:1157-1159, 1956	vitamin A capsules of 10,000 and 50,000 IU	orally	@ 160,000 - 180,000 units daily patient's comment with improvement she increased dosage	@ 7 mos	bone and joint pain, fatigue, insomnia, swelling of ankles, ecchymosis, soreness of the mouth with blisters on the tongue, frequency of urination, hepatomegaly, tibial tenderness high serum vitamin A	self medication but previously initiated by a dermatologist's prescription for acne	1	21 yrs	F
20. R.W. Hillman, Amer. J. Clin. Nutr. 4:603-608, 1956	vitamin A aqueous emulsion- Aquasol A	orally and I.V.	@ 1,000,000 units daily and 2,000,000 units daily @ 1,000,000 units daily	@ 13 days and 1 day 25 days	clinical picture resembled that of accidental vitamin A poisoning	experimentally induced	1	40 yrs	M
21. D.W. Creek, K.J. McNiece & L.M. Nelson, Amer. J. Gastroenterol 29:169-172, 1958	vitamin A Aquasol A in 2 cases- unknown in 3rd	orally	1 pt took 150,000 units daily 2 pts took 200,000 units daily patient extended medical recommendation	over 2 yrs 1 pt over 2 yrs 1 pt over 5 yrs	alopecia, anorexia, malaise, petechial and ecchymotic hemorrhages into the skin and mucous membranes	initially prescribed by dermatologist, physician or ophthalmologist & treatment extended or dosage increased by patient	3	16 yrs 47 yrs 67 yrs	1 F 1 M 1 M

Table I

22. T.K. Oliver, Jr. & W.H. Havener, ★ Arch.Ophthalmol. 60:19-22, 1958 and ★ T.K. Oliver, Jr. in J. Dis. Child 95:57-68, 1958	vitamin A unreported source	orally	@ 200,000 units daily superficial non-pitting acne not improved significantly by vitamin A treatment	@ 10 mos	leg pain, scanty menses, scaling and cracking of lips, fissuring of corners of mouth, limp, dry hair, maculopapular eruption on trunk and desquamation of palms and soles, hyperirritability, moderate alopecia, early papilledema in both eyes, tenderness in extremities, high serum vitamin A	physician's prescription and self medication, denying advice of subsequent physician	1	14 yrs	F
23. G. Morrice, Jr., ★ W.H. Havener & F. Kapetansky JAMA 173:1802-1805, 1960	vitamin A unreported source	orally and I.M.	@ 90,000 units daily - 200,000 units daily patients received vitamin A as an acne treatment	@ 10 mos to 4 yrs	double vision, scaling lesions on hands and legs, fissures at corners of mouth, scaling of lips, alopecia, hyperirritability, 14 lb. weight loss, irregular menses, headache, nausea, anorexia, bilateral papilledema, somnolence, splenomegaly	physician's prescription and druggist's recommendation	3 (1 prev. reported by Oliver)	1[illegible] yrs	F
24. W.H. Stimson, ★ New Engl. J. Med. 265:369-373, 1961	vitamin A unreported source	orally	@ 100,000 units daily originally as an acne treatment	@ 5 yrs	abdominal pain, anorexia, nausea, fatigue, hip and tibial pain, hepatosplenomegaly, dry lips, leukopenia, sparse hair, high serum vitamin A	physician's prescription and self medication	1	32 yrs	F
25. W.K. Woodard, ★ L.J. Miller & O. Legrant, J. Pediat. 59: 260-264, 1961	vitamin A Trivisol	orally	@ 71,500 units daily misinterpretation of pediatrician's instructions	@ 4 mos	increased intracranial pressure, bulging fontanelle, vomiting, irritability, drowsiness, hyperostosis of clavicles, tender subcutaneous swellings, spotty alopecia	parental overdosing	1	4 mos	M

Table I

26. C.H. Pease, JAMA 182:980-985, 1962 *	vitamin A Navitol or oleum percomorph	orally	excessive dose of A + D concentrate (teaspoon range est. 50,000-500,000 units daily)	@ 6-14 mos	retardation of growth and early closure of epiphyses in addition to the acute symptoms of toxicity; growth of legs seriously impaired	parental overdosing teaspoonfuls misinterpreted in place of drops	7	13 mos 7 yrs	6 F, 1 M
27. C.F. Burgoon, Jr., J.H. Graham, F. Urbach & R. Musgnug Arch. Dermatol. 87:63-80, 1963	vitamin A Aquasol A	orally	@ 300,000 U.S.P. units daily-600,000 U.S.P. units daily	@ 5-7 mos	insomnia, anorexia, headache, pruritus, dry skin, scaling lips, elevated serum vitamin A	physician's prescription	3	16-46 yrs	2 M, 1 F
28. J. Soler-Bechara & J.L. Soscia, Arch. Internal. Med. 112:462-466, 1963 *	vitamin A tablets of 25,000 IU	orally	@ 75,000 - 150,000 units daily - 375,000 units daily	@ 8 yrs	fatigue, weight loss, bone and joint pains, bone tenderness, loss of body hair, pruritus, dry skin, hepatosplenomegaly, anemia, headache, and skin rashes	self medication to improve vision and for tiredness	1	39 yrs	F
29. J.H. Smith, Oral Surg., Oral Med., Oral Pathol. 17:305-307, 1964 *	vitamin A unreported source	orally	@ 300,000 units daily	@ over 6 mos	swollen, bleeding, and tender gingivae, dry, scaly lips, itching, painful shins, anorexia	self medication increasing prescription of physician by 6 times original potency	1	14 yrs	M
30. S.S. Bergen, Jr., & O.A. Roels, Amer. J. Clin. Nutr. 16:265-269, 1965 *	vitamin A numerous preparations	orally	@ 33,333 I.U. daily + 8,714 I.U. from food daily vague history by patient - patient's neurotic state judged to interfere with her ability to relate	@ 8 yrs	sparse, coarse hair, pale, dry, scaly skin, edema in lower leg, erythema and hemorrhages in leg, fissuring of shank of leg, tenderness of joints, pain in bones, high serum vitamin A	self medication a food faddist	1	62 yrs	F

Table I

31. R.F. Krause, Amer. J. Clin. Nutr. * 16:455-457, 1965	vitamin A unreported source	orally	@ 50,000 I.U. daily as supplement	@ 17 yrs	no obvious signs and symptoms of vitamin A toxicity; high vitamin A content in liver	self medication because it was "good for him"	1	79 yrs	M
32. R.I. Lecks & D. Baker, Clin. Pediat. 4: 32-37, 1965	vitamin A unreported source	orally	@ 100,000 units daily - 400,000 units daily	@ 14 mos	possible pseudotumor cerebri vitamin A intoxication symptoms	incorrect dose was given reason not clear	2	4-1/2 yrs 9-1/2 yrs	1 F, 1 M
33. M. Shatin, Arch. Dermatol. 92:331, 1965	vitamin A unreported source	orally	@ 400,000 units daily	@ 6 mos	papilledema in the left eye	physician's prescription for keratosis follicularis	1	42 yrs	M
34. R.J. Di Benedetto, JAMA 201:700-702, * 1967	vitamin A unreported source	orally	@ 600,000 units daily	@ 3 yrs	fatigue, pain in joints and legs, pruritic, dry, scaly eruption of skin, marked edema, sparse, coarse hair, alopecia, yellowish skin, palpable liver, high serum vitamin A	self medication for maxillary sinusitis	1	51 yrs	F
35. W.B. Shelley & D.M. Carter, Arch. Dermatol. 95: 652-653, 1967	vitamin A unreported source	orally	@ 250,000 units daily	@ 4-1/2 mos	high serum vitamin A, pain in bones, headache, nervousness, persistent diarrhea	physician's prescription for Darier's disease	1	16 yrs	M
36. J. Jowsey & B.L. Riggs, J. Clin. Endocrinol. 28:1833-1835, 1968	vitamin A unreported source	orally	@ 200,000 units daily	@ 1 yr, 6 mos	headache, subacute papilledema, fatigue, dry, scaling skin, cracked lips, muscle stiffness, generalized pruritic rash, chronic paronychia about the toenails, high serum vitamin A, increased alkaline phosphatase activity, bone changes	self medication following physician's prescription, 300,000 I.U. for 1 month	1	18 yrs	F
37. B.P. Lane, Amer. J. Pathol. 53:391-398, 1968	vitamin A unreported source	orally	@ 50,000 units daily- 5,000,000 units daily	@ 5 yrs	moderate prolongation of prothrombin time and increase in serum alkaline phosphatase activity	self medication a food faddist	1	24 yrs	M

Table I

38. J.A. Madsen & A. Linker, J. Pediat. 75: 843-852, 1969	vitamin A Aquasol A liquid or capsule	orally	@ 50,000 units daily - 65,000 units daily - 100,000 units daily	@ 4 mos - 14 mos	fatigue, irritability, hepatosplenomegaly, abdominal distension with massive ascites, high serum vitamin A, fall in serum albumin, increased seizures	physician's treatment for 4 different syndromes	5	3-1/2-18 yrs	1 F, 4 M
39. M.S. Fedotin, ☆ JAMA 212:628, 1970	vitamin A tablets 50,000 I.U.	orally	@ 150,000 units daily	@ 4 yrs	pseudotumor cerebri, papilledema and diplopia, high serum vitamin A	physician's prescription for acne 4 years previously	1	18 yrs	F
40. M.H. Feldman & ☆ H.S. Schlesinger, Arch. Neurol. 22: 1-7, 1970	vitamin A unreported source	orally	@ 100,000 units daily - 500,000 units daily	@ 3-1/2 - 4 yrs	headaches, cracking lips, facial eruption, palpable liver, papilledema, benign intracranial hypertension, diplopia, high serum vitamin A	incorrect dose given and self medication for skin condition	2	20 yrs	1 M, 1 F
41. A.D. Lascari & W.E. Bell, Clin. Pediat. 9: 627-628, 1970	vitamin A unreported source	orally	@ 200,000 units daily - 300,000 units daily	@ 1 yr	pseudotumor cerebri, papilledema, headaches, double vision	self medication as therapy for facial acne	1	15 yrs	F
42. E. Rubin, ☆ A.L. Florman, T. Degnan & J. Diaz, Amer. J. Dis. Child. 119:132-138, 1970	vitamin A cod liver oil + multi-vitamin drops	orally	@ 400,000 units-625,000 units weekly	@ 4-1/2 yrs	hepatosplenomegaly, hepatic disfunction, hypersplenism	parental overdosing, one pint of cod liver oil or 1-1/2 bottles of multivitamin drops weekly	1	6 yrs	F
43. M.D. Muenter, H.O. Perry & ☆ J. Ludwig, Amer. J. Med. 50: 129-136, 1971	vitamin A Aquasol A and unreported sources	orally	@ 100,000 I.U.-200,000 I.U. daily 400,000 I.U. daily, then 200,000 I.U.-300,000 I.U. daily	@ 1-1/2 yrs @ 1 yr @ 8 yrs	fatigue, dry, cracking skin, pain in bones, anorexia, pruritus, headache, high serum vitamin A, palpable liver, sparse hair	self medication following original prescription of 300,000 I.U. for one month or 100,000 I.U. for 3 months	1 1	18 yrs (previously reported by Jowsey) 52 yrs	F F

Table I

44. R.G. Wieland, F.H. Hendricks, * P. Aust Y Leon, L. Gutierrez & J.C. Jones Lancet 1:698, 1971	vitamin A unreported source plus multivitamin preparation	orally	@ 105,000 units daily and 300,000 units every 4th or 5th day + A&D ointment	@ 6 mos	lethary, swollen tender cervical lymph nodes, pply-dipsia, polyuria, hyper-calcemia	self medication for acne pt. also took vitamin D (400 U. daily)	1	16 yrs	M

Table I

45. L.B. Dickey & E.J. Bradley, Stanford Med. Bull. 6:345-348, 1948	vitamin A Navitol cod liver oil Vi-penta Squibb's vitamin A	orally	@ 400,000 U.S.P. units daily + butter and other food rich in vitamin A	@ 18 mos	pruritus, pain in upper extremities, swelling on scalp, restlessness, thin, coarse hair, hepatomegaly, tenderness of bones, high serum vitamin A, high alkaline phosphatase activity	parental overdosing. Child was also given vitamin D (14,000 + U.S.P. units daily)	1	26 mos	F
46. P.E. Rothman & E.E. Leon, Radiology 51:368-374, 1948	vitamin A oleum percomorph Vipenta	orally	@ 125,000 units daily 75,000 units plus daily	@ 13 mos @ 6 mos	pruritus, irritability, anorexia, wrist pain, alopecia, fissuring of lips, yellowish skin, painful extremities, difficulty in walking, rash, hepatomegaly, tenderness in limbs, high serum vitamin A	parental overdosing, vitamin D was also given (18,410 units daily)	2	14 mos 22 mos	1 M, 1 F
47. Case No. 623, In Case Reports of Children's Memorial Hospital, Chicago 9:1831-1833, 1951	vitamin A oleum percomorph ABDEC drops	orally	@ 100,000 units daily - 115,000 units daily	@ 9 mos @ 6 mos	irritability, refusal to walk, erythematous, scaly rash on extremities and buttocks, high serum vitamin A, lymphadenopathy, cortical hyperostoses, poor appetite, listless, pruritus fever	parental overdosing. Child was also given vitamin D (14,400 + units daily)	1	15 mos	F
48. J. Caffey, Amer. J. Roentgenology 65:12-26, 1951 (cases were previously reported by J. Caffey in Pediatrics 5: 672-688, 1950.)	natural vitamin A oleum percomorph Drisdol + A	orally	@ 100,000 - 600,00 I.U. daily	@ 6 mos - 17 mos	infantile cortical hyperostosis, increased serum vitamin A	parental overdosing, gave oleum percomorph instead of cod liver oil. Three children also received vitamin D (20,000-40,000 units daily)	7	12 - 37 mos	5 M, 2 F

Table I

49. A.L. Kane, Arizona Med. 9: 29-31, 1952	vitamin A Theragran capsules 25,000 IU	orally	@ 50,000 - 100,000 units daily + milk, butter, green or yellow vegetables	@ 1 yr oleum percomorph Nomicebrin + Vigraine capsules prior to 1 year	hepatomegaly, discrete excoriated macular skin rash, high serum vitamin A	parental overdosing mother a registered nurse	1	8 yrs	M
50. _____, Penn. Med. J. 55: 933-934, 1952 (cites case of G.C. Meyersbach, et al; New Engl. J. Med. 246:978-980, 1952)	vitamin A oleum percomorph	orally	@ 240,000 units daily	@ 1 yr	anorexia, irritability, pruritic skin rash, subcutaneous tender swelling, pain of extremities, cracked dry lips, sparse, coarse hair, cortical hyperostosis, and a high serum vitamin A	doctor's prescription for rickets. Child also had an avid craving for butter	1	3 yrs	F
51. M.T. Harrison & R.D. Mercer, Cleveland Clin. Quart. 20:424-429, 1953	natural vitamin A oleum percomorph	orally	@ 200,000 - 400,000 units daily	@ 27 mos	hyperirritability, cheilosis, pruritus, swelling along ulnas and fifth metatarsals, high serum vitamin A	parental overdosing	1	28 mos	M
52. J.D. German, JAMA 155:947, 1954	vitamin A unreported source	orally	@ 50,000 - 100,000 units daily	@ 8 mos	astereognosis and onycholysis not judged to be due to vitamin A toxicity	incorrect dose was given no reason given for dosage	1	50 yrs	F
53. H.S. Bloch, Minnesota Med. 38: 627-632, 1955	vitamin A unreported source	orally	@ 50,000 units daily suspected solvent vapors, patient's report - a house painter	@ 3 yrs	weakness, headache, anorexia, fever, hepatomegaly, absent patellar reflex on the left and atrophy of the quadriceps muscle, neurtic pain in left hip and thigh, intestinal bleeding	physician's prescription and continued self medication for eczema	1	54 yrs	M
54. R.B. Tudor, Journal Lancet 75: * 372-373, 1955	vitamin A Navitol with viosterol	orally	@ 200,000 units daily	@ 8 mos	craniotabes; irritability, sparse hair, high serum vitamin A	parental overdosing	1	20 mos	M

Table I

55. C.A. Turtz & A.I. Turtz, ☆ Amer. J. Ophthalmol. 50:165-166, 1960	vitamin A unreported source	orally	@ 200,000 units daily	@ 18 mos	headaches, blurred vision, occasional attacks of diplopia, malaise, pain in joints, superficial hemorrhages throughout the retinas of both eyes, early edema of left disc	incorrect dose given self medication for acne	1	17 yrs	M

Table I

56. W.T. McLean, Jr., Clin. Res. 20(1): 113, Jan., 1972	vitamin A unreported source	orally	@ 150,000 - 200,000 I.U. [illegible]y	@15 mos - 26 mos	papilledema, headache, vomiting, high serum vitamin A levels	incorrect dose taken reason not clear	2	adolescents	F
57. R.M. Restak, J. Nerv. Ment. Dis. 155(1):72-75, 1972	vitamin A Hal-Sal	orally	@ 100,000 - 150,000 units daily	@ 6 mos +	depression, insomnia, anorexia, weight loss of 17 lbs., blurred vision, hyperacusis, ataxia, daytime lethargy, toxic psychosis, frontal headaches, amenorrhea, papilledema, high serum vitamin A levels, pseudo-tumor cerebri	incorrect dose taken self-medication for acne	1	18 yrs	F
58. N.J. Siegel & T.J. Spackman, Clin. Pediat. 11(10):580-584, 1972	vitamin A unreported source	orally	@ 25,000 - 57,000 I.U. daily Mother of one a health faddist	@ 9 mos - 1 yr	anorexia, irritability, lethargy, vomiting, stiff neck, inability to walk, increased head size, patchy alopecia, exfoliative pruritic rash, pain in shins, slightly enlarged liver and spleen, elevated transaminase level, elevated serum Ca, markedly elevated serum vitamin A, low protein conc. in CSF, bulging anterior fontanel, increased intracranial hypertension	parental overdosing. One child also received daily 1,000 I.U. of vitamin D, 200 I.U. of vitamin E, 480 mg of vitamin C, 1,600 mg of Ca and 750 mg of PO_4	2	1 yr - 2-1/2 yrs	1 M, 1 F
59. H.L. Greene, Drug Intelligence and Clin. Pharm. 6: 355-360, Oct., 1972	vitamin A multi-vitamin drops	orally	@ 12,000 I.U./day for 7 days an infant of 2100 grams	@ 7 days	increased liver size to 4 centimeters below costal margin, bulging fontanelle, several episodes of projectile vomiting over 8 days, white count was 3,000/cu ml. with 30% neutrophils, hemoglobin was 8.4gm/100ml	incorrect oral dose given inadvertantly	1	infant	F

Table I

60. P.M. Galpke, Can. Med. Assn. J. 104:533, Mar. 30, 1971 *	vitamin A tablet 50,000 I.U.	orally	@ 200,000 units daily taken for acne	@ 2 yrs	headaches, vomiting, diplopia, strabismus, papilledema, CSF pressure grossly elevated	incorrect dose given by pharmacist without time limit	1	15 yrs	F
61. J. Marie & G. See, Amer. J. Dis. Child 87:731-736, 1954 *	vitamin A Vitadone Forte nose drops 50,000 IU/8	orally and nasally (nosedrops)	@ 300,000 - 350,000 units daily	@ 1 - 6 days	vomiting, paleness, lethargic, bulging fontanel, crying, diarrhea, edema	parental overdosing. Four of the patients also received 300,000 units of vitamin D	5	2-7-1/2 mos	1 F, 4 M
62. G. Frontali, Schweiz. Med. Wochenschr. 82(15): 430-433, Apr. 12, 1952 *	vitamin A Asteril	orally	@ 60,000 units daily - 75,000 units daily	@ 214 days @ 100 days	intracranial pressure, projection of the forehead, periosteal thickening of the skull-cap and long bones (cortical hyperostoses) hemorrhagias, anemia, hypoproteinemia, Takata-positive	incorrect dose given. Patient also received 40,000 I.U. of vitamin D daily	1	4 yrs	F
63. J.D. Pickup, Arch. Dis. Child. 31(157):229-232, June, 1956 *	vitamin A avoleum	orally	@ 463,040 units daily - @ 347,280 units daily	@ 42 days @ 730 days	vomiting, anorexia, pain in arms, legs, and forehead, insomnia, weight loss, scaling of skin, cracking of lips, bleeding of lips, enlarged liver and spleen, conjunctivitis, edema of face, alkaline phosphatase elevated, high serum vitamin A levels, shedding of hair, skin rash, elevated plasma Ca and P	incorrect dose given, originally prescribed by a dermatologist and expanded by the Mother	2	4-6 yrs	1 M, 1 F

Table I

64. J. Lyon & J.W. Paulley, Brit. J. Dermatol. 76(2):92-93, 1964	vitamin A unreported source	orally	@ 600,000 units daily lower quantities taken earlier in life	@ 365 days+	headache, tinnitus, vomiting, unsteady gait, papilledema associated with hydrocephalus, lethargic, aching in legs, blurred discs, wasting and weakness of lower limbs, dizzy, some wasting of interossei muscles of the hand	incorrect dose taken for skin condition origin of use and history not clear	1	12 yrs	M
65. W. Raaschou-Nielsen, Dermatologica 123:293-300, 1961	vitamin A palmitate Arovit	orally	@ 300,000 I.U. daily	@ 365 + days	anorexia, weight loss, falling hair from scalp, dry brittle hair, eyebrows and pubic hair thinned, skin felt dry and itchy, fissures of mouth and nostrils, alkaline phosphatase elevated, high serum vitamin A	physician's prescription for skin condition	1	18 yrs	F
66. G. Goeckenjan, et al, Deut. Med. Wochenschr 97: 1424-1429, 1972	vitamin A Maisin Hochkonsentrat	orally	@ 4,000,000 I.U.	@ 22 days	headaches, dizzy, visual disturbances, vomiting, body weakness, itchy skin, lip and gum changes, scaling of skin, clouding of consciousness for 4 weeks, acute renal failure, hyperglycemia, aplastic anemia, severe infectious complications, high serum vitamin A, hepatomegaly, hypoprothrombinemia, hypercalcemia, hyperlipidemia	physician's prescription for psoriasis	1	30 yrs	M
67. O.F. Jillson, Arch. Dermatol. 93:484-486, April, 1966	vitamin A unreported source	orally	@ 500,000 units daily	@ 60 days	headache	physician's prescription for Darier's disease	1	39 yrs	F

Table I

68.	B. Persson, R. Tunelland K. Ekengren, Acta Paediat. Scand. 54:49-60, Jan. 1965	vitamin A AD-vimin, Astra A-D-ol aquosum	orally	@ 17,500 - 60,000 I. U. daily	@25 - 98 days	anorexia, hyperirritability, edema in head, bulging fontanels, "Sun set" gaze, alkaline phosphatase elevated, high serum vitamin A, exophthalmus, craniotabes, widening of metaphyseal ends, apathy	physician's prescription and parental overdosing, patients also received 3,600-9,000 units daily of vitamin D	5	2-1/2 mos - 5-1/2 mos	2 F, 3 M
69.	P. Ammann, K. Herwig & Th. Baumann, Helv. Paediat. Acta 23(2):137-146, 1968	vitamin A palmitate Arovit	orally	@ 150,000 I.U. daily	@ 730 days	lethargic, anorexia, headaches, vomiting, slight fever, nose bleeds, dry, fissured lips, pain in arms and legs, dry, scaling skin, coarse hair, immobility, elevated alkaline phosphatase, slight hypercalcemia, high serum vitamin A, bone changes, hepatomegaly, hypoprothrombinemia	incorrect dose was given parental overdosing	1	7 yrs 2 mos	M
70.	W. Ehrengut, Z. Kinderheilk. 77(4):468-482, 1955	vitamin A palmitate Arovit	I.M. and orally	@ 187,000 I.U.	@ 2 days	opisthotonus, bulging fontanel, somnolence, moderate edema, petechiae in the face, purulent rhinitis, keratomalacia, hepatorplenomegaly, severe redness of tongue and throat, weight loss, CSF pressure greatly elevated	incorrect dose given. Patient also received 200,000 I.U. of vitamin D	1	4-1/2 mos	M

Table I

71. J.W. Smit & D.P. Hafstede, Ned. T. [illegible]esk 110:10-1[illegible] 1966	vitamin A unreported source	orally	@ 150,000 - @ 300,000 Units daily	@ 18 mos @ 4 yrs	psychic changes, menstrual disturbances, insomnia, thirst, pruritis ani, dryness of skin and mucous membranes, fissuring of lips, falling hair, epistaxis, slight abduction paresis, increased CSF pressure, anemia, leucocytosis, elevated serum phosphatase, feeling of pressure in ears, diffuse pigmentation in the face with hyperkeratosis	self-medication	2	20 - 24 yrs	2 F
72. P.G.I. Jennekens & * C.W.M. Van Veelen, Presse Med 74: 2925-2928, 1966	vitamin A unreported source	orally	@ 200,000 - 300,000 Units daily	@ 56-913 days	headache, insomnia, hyperirritability, menstrual irregularities, pruritus, urinary incontinence, epistaxis, back joint and extremity pain, diplopia, papilledema, desquamation of the skin, fissuring at corners of mouth, erythema, weight loss, anorexia, EEG - anomalies, hepatomegaly, elevated serum alkaline phosphatase, hemorrhage of fundus, moderate elevation of CSF, slight acceleration in the sedimentation rate, vomiting and nausea	physician's prescription	2	19 - 21 yrs	2 F

Table I Supplement

HYPERVITAMINOSIS A in MAN

	Author(s) and Reference	Form of Product	Mode of Administration	Estimated Dosage	Duration	Toxicity (salient symptoms)	Cause, Origin or Reason for Toxicity	No. of Pts.	Age	Sex
73.	H. Pinkus & R. Hunter, J. Invest. Dermatol. 42:131-136, 1964	vitamin A Vi-Dome-A oral tabs	orally	@150,000 units daily	@ 30 days	retardation of maturation of human keratinocytes	experimentally induced	10	25-40 yrs	7 M, 3 F
74. ★	J.P. Nater & H.M.G. Doeglas, Acta Dermatovener. 50:109-113, 1970	halibut liver (not oil)	orally	@ 2-30,000,000 units daily	@ 1 day	headache, nausea, vomiting, desquamation of face, trunk, hands and feet, immobility, high serum vitamin A levels, elevated lipoid and cholesterol levels, slight increase in LDH	ate too much halibut liver	11	23-61 yrs	11 M
75. ★	S. Silverman, Jr., et al, J. Oral Ther. Pharmacol. 2(1):9-23, July, 1965	vitamin A Vi-Dom-A tablets for oral leukoplakia	orally	@ 600,000 units daily	@ 35 days	dry, itchy, scaly skin, skin rash, photosensitivity, urinary retention, high serum vitamin A levels, altered liver function (elevated BSP & SGOT)	physician's prescription for oral leukoplakia	6	33-83 yrs	2 M, 4 F
76. ★	J. Caffey, Amer. J. Dis. Child. 79:404-405, 1950 (Dr. H.W. Josephs mentioned)	parcomorph liver oil	orally	large amounts			infantile cortical hyperostosis	4	infants	

- has examined 4 more cases since his first report, (Amer. J. Dis. Child. 67:33-43, Jan., 1944)

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77. ★	J.M. Cluet-Garcia, Acta Ped. Espan. 9:1448, Dec., 1951		orally	massive doses of vitamins A and D		benign hydrocephalus		1	infant	
78. ★	S.J. Yaffe, et al, Pediat. 48: 655-656, Oct., 1971	general paper; high potency vitamin A preparations can cause serious side effects if taken in excess								
79.	H.R. Getz, et al, JAMA 112(14): 1308-1311, April 8, 1939	vitamin A halibut liver oil for TB	orally	@ 2,000,000 units daily	@ 1 day	dull headache	physician's prescription	4		
		vitamin A as carotene	orally	@ 2,000,000 units daily	@ 1 day	dull headache	physician's prescription	1		
80.	T. Dull, et al, J. Clin. Investig. 40:1035, 1961	vitamin A unreported source	orally	@ 200,000 units daily	@ 3 - 4 wks	high serum vitamin A, depressed serum and urinary citrate, decreased serum and urinary calcium, decreased urinary phosphorus	experimentally induced	6 subjects		
81.	J. Cleland & R.V. Southcott, Med. J. Aust. 1(26):1337-1342, 1969	vitamin A husky (dog) liver	orally	large amounts	@ 3 wks	severe skin desquamation, fits, gastrointestinal pain, dysentery, hair loss, anorexia, vomiting, delirium	ate large amounts of husky liver	2 subjects		2 M
82. ★	C. Morrice, JAMA 213: 1344, Aug. 14, 1970	Review paper; refers to papers by Fedontin, Oliver and Havener and Morrice, et al.								

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83. J.R. Frey & M.A. Schoch, Dermatologica 104(2):80-86, 1952	vitamin A acetate Arovit for psoriasis	orally	@ 400,000 - 3,000,000 IU/d	@ 2 days - 6 mos	dryness of the lips, fissuring of the lips, headache, hyperirritability, nausea, scaling of the skin, depapillation and redness on tip of tongue	physician's prescription	9		
84. C.M. Katz & M. Tzagournis, Metabolism 21(12):1171-1176, Dec., 1972	vitamin A for severe acne unreported source	orally	@ 200,000 units daily	@ 2 yrs	anorexia, lethargy, weakness, vomiting, gingival bleeding, 10-lb weight loss, nausea, headaches, stiff shoulders, fasciculation in lower extremities, flaky pruritic rash, epistaxis, loss of some scalp hair, pigmentation of lower abdomen, polyuria, polydipsia, dry, cracked lips, hypercalcemia, tender, palpable liver, EKG showed shortened QT interval and flattened T waves, elevated alkaline phosphatase, high serum vitamin A	self-medication for severe acne	1	18 yrs	M

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March 12, 1973

Miss Beryl McCullar
Hearing Clerk
Food and Drug Administration
Room 6-88
5600 Fishers Lane
Rockville, Maryland 20852

Re: Proposed Statement of Policy
Vitamins A and D, 37 F.R. 26618.

Dear Miss McCullar:

Enclosed are five copies (in four volumes) of comments by Vitaminerals, Inc. on the proposed statement of policy dealing with Vitamins A and D [37 F.R. 26618, December 14, 1972]. Mr. Brandenburg, of the Office of the Associate Commissioner for Compliance, advised the undersigned that these comments could be filed through March 13, 1973.

This submission is divided into four volumes. Volume I contains a summary of Vitaminerals' evaluation of the various articles cited by the Food and Drug Administration, and the additional articles uncovered by Vitaminerals, dealing with the toxicity of Vitamin A. Also included in Volume I are reprints of all the articles collected by Vitaminerals reporting on human toxicity in Vitamin A. Volume II contains reprints of all the FDA authorities, including the FDA animal reports, on Vitamin A. Many of these articles are duplicates of the studies reported by Vitaminerals in Volume I, but are included in the interest of completeness and so that reviewing officials at the FDA can readily cross-reference both volumes in order to confirm the completeness of the work done by Vitaminerals.

Volume III contains Vitaminerals' summary of all the toxicological reports on Vitamin D, as well as the reprints of the articles on Vitamin D as obtained by Vitaminerals.

Volume IV contains reprints of the FDA's articles on Vitamin D, including the animal studies referred to by FDA. Again, Volume IV contains some duplication of the data reported in Volume III, but for the same purpose as before.

Briefly, here is the situation as Vitaminerals sees it. First, with respect to Vitamin A.

VITAMIN A

The preamble to the FDA's proposed statement of policy states that doses of 50,000 I.U. in adults and 20,000 I.U. in infants on a daily basis over long periods are known to produce toxicity. The authorities cited by the FDA and those developed by Vitaminerals support no such allegation. First of all, there are no reported fatalities whatever with Vitamin A at any dosage level. Next, many of the references cited by the FDA are, by their nature, irrelevant to the question of human toxicity. These relate either to experimental studies (incidentally, where no ill effects were shown) or to a bizarre incident where some fishermen ate halibut liver in which the Vitamin A dosage ranged from 2 million to 30 million units in a single dose - hardly a relevant basis for deciding the dietary patterns of the American population.

The remaining studies, involving 64 individuals over a 33-year period, include many cases where the subjects were taking Vitamin A under the prescription of a doctor at very high levels to treat disease conditions. In other words, the doctor was deliberately approaching a very high level of Vitamin A intake in order to achieve a specific result for patients under his care. This would contradict the FDA's argument that the safety of Vitamin A can only be assured by limiting it in high dosages to prescription uses. The side effects cited by FDA in effect were caused by prescription usage and have nothing to do with over-the-counter purchases. Presumably they could occur as well after this regulation as before and the regulation does not purport to reach the problem of using toxic doses in prescription drugs. In any event, the levels ingested were, as the tables in Volume I point out, extremely high, ranging from levels of 100,000 units per day to over a million, and therefore have nothing to do with doses of 50,000 and 20,000 which, FDA says, produce toxic effects.

Moreover, as Vitaminerals points out in Volume I, page 5, many of the toxic reactions were related to peculiar products no longer on the market. One was similar in appearance to cod liver oil and therefore was often mistakenly dispensed, by both physicians and parents, as if it were cod liver oil. Another product was marketed in an ampule which contained 350,000 units, and, because it was in ampule form, appeared to be a single dosage unit, which it was not. Both of these products were reformulated and the problem of potential Vitamin A toxicity disappeared.

Thus, it would appear that the Vitamin A toxicity reports either occurred in prescription usage (where this proposed regulation would offer no protection) or in peculiar product situations no longer in existence, and therefore have no bearing whatsoever on the statement quoted above by the FDA about the level of toxicity of Vitamin A.

One of the studies [H-26, Volume II] deserves special mention. Here the FDA would suggest that the condition of shortening of the leg in infants was caused by dosages of Vitamin A. An examination of the study reveals that it does not support such a conclusion. Seven children are reported on who suffer from this condition. The levels of Vitamin A range from none, in the case of one infant, up to 500,000 units in another. A third infant was receiving the recommended dietary allowances, and the remainder much higher levels, with one unknown. With such a broad range of dosage figures it is obviously scientifically impossible to implicate Vitamin A as the culprit in this situation. Vitamin A is not a constant in these reports.

The FDA also cites a number of animal studies (some of which, mysteriously enough, report on Vitamin A deficiency problems, a subject wholly unrelated to the proposed regulation.) However, animal studies are relevant only if a relationship between the dosage ingested by the animal in a test and a quantitatively anticipated dose in humans can be established. The FDA, in its proposed statement of policy, fails to translate any of the animal data work into human levels. Vitaminerals has, however, done this for each of the studies [Volume I, page 8]. These reveal equivalent dosage levels that are so high as to be meaningless to any human toxicological problem. They range from a low of 4.8 million daily units to a high of 81 million units of Vitamin A.

From all this it can be seen that there is no toxicity data reported by FDA, or discovered by Vitaminerals, which supports any such maximum level as required by the proposed regulation. The incidences of toxicity reported are either irrelevant or at levels tenfold higher than that suggested by FDA to be the case.

VITAMIN D

The Vitamin D data is summarized in Volume III and covers the references cited by the FDA and the additional ones discovered by Vitaminerals. The studies report on 152 subjects over a 32-year period. However, the subjects in study H-1 [Vol. II] must be rejected from evaluation because they were under an experimental efficacy study and, in any event, they suffered no side effects. In another study [D-24, Vol. III], the subjects were not specific and the report does no more than analyze a method for determining a control dose of Vitamin A under prescription for hypocalcemia. The elimination of these two studies leaves 113 subjects for evaluation, and an analysis of those patients appears in Volume III, pages 2 and 3. The great preponderance of these subjects were receiving Vitamin D on prescription, and thus the proposed regulation, limiting OTC usage, would have offered them no protection whatever.

The FDA's suggestion in its preamble that the daily ingestion by infants of dosages between 1,000 and 2,000 I.U.'s has produced hypervitaminosis D is invalid. It is particularly invalid if, as the FDA intimates, a conclusion is drawn that that dosage level is a toxic level. Actually, as the study shows, the reactions cited by FDA occurred in infants who received no Vitamin D [H-3, H-6, D-2, D-26], as well as in infants who were receiving the RDA levels of Vitamin D [H-3].

The agency implies that Vitamin D is a causative factor in infantile hypercalcemia or idiopathic hypercalcemia. (The references cited by the agency are to both). Such an implication is not justified. A thorough and careful analysis of the cited documents reveals that those conditions are

probably genetic in origin and not caused by any specific substance. While it is true that in some of the reports the authors conclude that Vitamin D is associated with these conditions, a careful reading of the actual report reveals a lack of factual support for any such conclusions. The reactions associated with these conditions can occur with no Vitamin D, sub-normal amounts of Vitamin D, RDA levels of Vitamin D, calcium and other substances. Thus, what is implicated here is the presence of Vitamin D in certain unfortunates suffering from this disease condition and the so-called toxic level of Vitamin D has nothing to do with the individual's problem. For these unfortunates the issue is not to avoid a toxic dose of Vitamin D but to avoid it altogether - just as they should avoid calcium (for which FDA sets no maximum limits) and many other substances.

The animal work cited by the FDA is as valueless as the animal work cited for Vitamin A. Translating the figures to anticipated human dosage would develop totals of between two to four million units in one study, and 37.5 million units per day in the other.

Finally, a great many of the articles cited by the FDA are mere reviews of the other articles and, as such, contribute no new specific data. Accordingly, they are not discussed in detail.

In sum, what Vitaminerals has presented is a detailed evaluation, with appropriate charts, of each of the animal and human studies cited by the FDA and those developed by the company. Such an analysis reveals that the levels of ingestion presented by the FDA in the proposed regulation are not toxicologically significant. Since there is no scientific or toxicological basis for the limits imposed by the FDA (the only basis sought here by FDA) we suggest that they are factually unsound and therefore statutorally impermissible.

Very truly yours,

William R. Pendergast

Enclosures
WRP/bmd

INTRODUCTION

The following comments regarding the proposed statements of policy, Food & Drug Administration, as published in the Federal Register, Volume 137, Number 241, Thursday, December 14. 1972, are herewith filed by Vitaminerals, Incorporated, 1815 Flower Street, Glendale, California 91201.

To facilitate ease of review, we are filing these comments, statements and objections in four separate categories which correspond generally in form to the sequence of statements setforth in the publication in the Federal Register.

I Vitamin A - Human Study

II Vitamin A - Animal Study

III Vitamin D - Human Study

IV Vitamin D - Animal Study

Where references are made to papers, which were not included in the Food & Drug Administration's Bibliography, copies of the complete papers referred to are contained.

As set forth in the Federal Register (Volume 27, Number 241, December 14, 1972) the Food & Drug Administration contends the availability of vitamin A in "high dosage levels without prescription, contributes significantly to their misuse and the occurrence of serious adverse effects". The statement is further made that vitamin A, at levels of 50,000 International Units per dosage unit, is available over-the-counter. Both of these statements are incorrect and not substantiated by the data, either presented in the bibliography or in the Food & Drug Administration's own prior regulation.

The Food & Drug Administration has previously published in the Federal Register, August 19, 1971, new regulations placing 50,000 units vitamin A products on a prescription basis only. These regulations have been in effect since December, 1971. At the present time vitamin A is not available over-the-counter at 50,000 I.U.'s, but contrary to the statement by the Administration, is only available at this level under a prescription legend. The purpose of this limiting regulation, as stated by the Administration when proposed, raised no question of danger to public health, nor serious adverse effects. We respectfully submit, therefore, that the specific statement and the inferences made by the Food & Drug Administration in the proposed regulations of December 14, 1972, are incorrect and are not substantiated by fact.

To support the overall contention of the proposed regulation, the Food & Drug referred to a substantiating bibliography covering the period 1938 to 1971. The following analysis encompasses both this bibliography, supplied by the Food & Drug Administration, and additional references researched by Vitaminerals, Inc. We believe these to be comprehensive and have taken the figures and facts presented by the Government and by additional papers to provide the following analysis:

HUMAN STUDIES

One Food & Drug Administration reference was incorrectly identified in the published list (17 - Government Hypervitaminosis A). One paper (9) was unobtainable. Two were (A2 and A27) supplied by Vitaminerals, Inc., and not included on the FDA list.

The references, FDA and Vitaminerals, Inc., covered a 33-year-period - from 1938 to 1971 - and incorporate reports on 145 subjects. This is the bibliography the government contends establishes availability of vitamin A over-the-counter as contributing to adverse effects.

(Note: FDA reference numbers, Hypervitaminosis A are proceeded by "H" to differentiate human studies from animal studies. Vitaminerals' reference numbers are proceeded by "A".

The following had no connection with the Food & Drug's statement, nor this proposed rule making:

l Fishermen (H39)	These men suffered from adverse effects by ingesting Halibut liver freshly caught aboard their fishing boat.
4 Infants (A26)	These subjects were on an experimental study of vitamin A intake under prescription. There were no ill-effects!
ix Adults (H32)	This was an experimental study on prescription at massive levels which provided some mild effects and is not germane to the question posed.
n Adults (A13)	This was an experimental study of vitamin A under prescription showing no ill-effects at high levels.

These three experimental studies and an ingestion of Halibut liver cannot rationally be included in reference to the FDA statments and intent.

The remaining 64 subjects covered in the bibliography fall into five groups:

1) Vitamin A dosage on prescription
2) Vitamin A dosage probably on prescription
3) Vitamin A dosage on prescription with an additional continuing intake or increased level
4) Self prescribed
5) Unknown

1) 16 Subjects: These subjects were taking vitamin A under prescription and while under the supervision of a doctor (References: A2, H7, H10, H13, H18, H21/20/41, H25, H28, H34, A45, H38, H37.

2) 15 Subjects: These subjects were probably taking vitamin A on prescription or direction of their physicians. They were infants and on supplements normally prescribed by pediatricians. Additionally, their intake started at birth when they would be under the care of a pediatrician (Reference: A44).

3) 18 Subjects: These subjects were initially treated with vitamin A under prescription. As noted in the attached summary sheets, they continued use on their own volition; they increased dosage levels of their own volition, they resumed dosage of vitamin A on their own volition, and the dosages was subject to mistake in directions (References: A2, H1, H12, H15, H16, H18, H19, H24, H26, H29, H30, H36).

4) 10 Subjects: These subjects instituted vitamin A therapy of their own vo-

lition, utilizing over-the-counter preparation (References: A1, H14, H22/41, H33, H23, H27, H35, H40, A40, H45).

5) Four Subjects: These four subjects had no known source or specific cause (References: H26, H37).

In review, over a period of 33 years 64 subjects are referred to as being on massive dosage of vitamin A over extensive periods of time. Of these, ten instituted vitamin A dosage of their own volition, four are of unknown origin, 18 continued or modified vitamin A dosage after iniating it under prescription and professional supervision. It would seem the government's contention is difficult to substantiate in light of these actual figures and statements.

DISCUSSION

All the previous referred to subjects were reported on massive vitamin A intake in excess of the unitage levels stated by the Food & Drug Administration. The bibliography does not even support the previous restriction on 50,000 units of vitamin A dosages, even though it was promulgated without reference to potential harm or danger to public health. A comprehensive review of the papers discloses further pertinent facts bearing on this matter.

22 subjects, all of whom received massive dosages of vitamin A under prescription, were utilizing the vitamin product, Oleum Percomorphum, or its equivalent. The majority of the cases established the fact that the similarity of appearance of the product and the package to Cod Liver Oil led to a mistake in directions and the dosage at the "traditional" Cod Liver Oil level, i.e., 1 teaspoonful. At this erroneous dosage and the concentration, A intake was generally between 200,000 to 500,000 I.U.'s, the same pattern of dosage and product follows in the remainder of the papers although not specifically

stated. The error in dosage level was made by mother, druggist, doctors, and in several cases the hospitals. This led to the removal of the product from the market in the early 1950's and its replacement with obvious drop dosage forms to prevent misinterpretation. This cause and the success of removing a packaging and appearance problem can be emphasized by the lack of reported infant cases following that date some 20 years ago (References: A44, A2, H10, H12, H26, A21).

Three infants were reported affected by massive (350,000 I.U.'s) doses of vitamin A prescribed by physicians. The unique packaging, glass ampules, led to overdoses. Because of their appearance the mother considered an ampule as a single dose; since once opened, it was not readily resealable, the entire content was given in single dosages. Two additional infants were purposely given the same dosage, while hospitalized, to duplicate the symptoms. At the suggestion of the pediatrician the product was reformulated to a level of 70,000 units per ampule and "no further problem was encountered" (Reference: H15).

Eight of the subjects took vitamin A over-the-counter at their own volition. The majority of these were dermatological problems, colds, and in two cases one was a food allergist and the other was a psychiatric patient. The most common cause in the remaining subjects was continuation of programs originally prescribed by dermatologists.

In summary, the above and attached analysis of subjects on massive dosages of vitamin A failed to establish the Food & Drug Administration's contention with regard to potential hazards from over-the-counter vitamin A products. An analysis of the papers shows exactly the opposite to be true; that the product, at reasonably high potency levels over-the-counter, provides an exceptional margin of safety. Taken in context with the fact that 2 1/2% of the infants in this country, 2 1/2% of the children in this country, and almost 5% of the adults in this country will suffer mild to severe

eactions from milk, we believe that the safety of reasonably high dosage of vitamin A ver-the-counter, has been well established.

PROPOSED POTENCY LEVEL - VITAMIN A

The statement is made by the Food & Drug Administration that doses of 50,000 U.'s for adults and 20,000 I.U.'s in infants on a daily basis over long periods of me are known to produce toxicity. The average adverse dose level in the referred pers for infants is 200,000 I.U.'s per day for 8.4 months. The average level for ildren is 270,000 I.U.'s per day for 26 months. The average level for adults is 3,000 I.U.'s per day for 3.2 years. The minimum in all three categories exceeds e government's figures and in one case (Reference: A32) the 50,000 I.U. level was intained for 17 years with no untoward effect.

FDA ANIMAL STUDIES

Included in the bibliography under vitamin A Tetrogenicity (referred to as AA ference in summaries attached) were animal studies. With readily available human a on vitamin A levels available, Vitaminerals, Inc., did not pursue papers deal- with animal work. A review of the animal studies is attached. The Food & Drug inistration's bibliography shows six papers not germane to the proposed regulation. r papers (Reference: AA1, AA3, AA7 and AA16) deal with the effects of vitamin A de- iency on animals. One paper (AA23) cannot be realted to any dosage levels and the al paper (Reference: AA26) discussed vitamin A Acid, not vitamin A.

The animal studies are not meaningful in a direct reference to human effects as itted in the papers. This also has been the position of the Food & Drug Adminis-

FDA ANIMAL STUDIES

ration with regard to all submitted animal studies. Therefore, little or no actual information can be drawn from them and in light of existing human studies the data presented is of no import. However, one interesting fact should be noted. If the animal level were translated into approximate human levels, based on a 100 lb. female, the following would be the relative vitamin A intake for a human.

FDA REFERENCE

AA2:	81 million units
AA5:	8.5 million units
AA8:	7.2 to 14.4 million units
AA11:	4.8 to 7 million units
AA12:	24 million units
AA14:	9.6 million units
AA15:	23 million units
AA17:	14 million units
AA18:	6 million units
AA21:	4.5 to 18 million units
AA25:	11.5 to 115 million units

A RATIO OF POTENCY THAT COULD NOT EVEN BE DESCRIBED ADEQUATELY AS MASSIVE.

SUMMARY & RECOMMENDATION

The foregoing data demonstrates the lack of potential harm of vitamin A over-the-counter in adult products. At levels of 50,000 International Units per unit dose, now restricted to prescription, this data holds true. It would seem unwarranted and illogical to promulgate further regulations based on unsupported statements. The

hest level of vitamin A generally available over-the-counter since 1971 has been
000 units per unit dose, the safety of which has obviously been well established.

It's our contention that the current, normal maximum levels of vitamin A gen-
lly available without prescription, i.e., 25,000 units per day, per dosage unit,
uld be maintained and provide qualified and proven safe levels.

As set forth in the Federal Register (Vol. 27, No. 241, December 14, 1972), the Food & Drug Administration contends that the availability of vitamin D in an excess of 400 International Units per dosage unit, available without prescription, could cause the possibility of severe irreversible adverse effects.

To support this statement, the Food & Drug Administration referred to a substantiating bibliography covering the period 1938 to 1970.

The following analysis covers both this bibliography, supplied by the Food & Drug Administration, and the additional references researched by Vitaminerals, Inc. We believe these to be comprehensive and have taken the figures and facts presented by the government, and by additional papers, to provide the following analysis:

HUMAN STUDIES

The references, FDA and Vitaminerals, Inc., covered a 32-year-period - from 1938 to 1970 - and incorporate reports on 152 subjects. This is the bibliography the government contends establishes availability of vitamin D over-the-counter as contributing to adverse effects.

(Note: FDA reference numbers, Hypervitaminosis D, are preceded by "H" to differentiate human studies from animal studies. Vitaminerals reference numbers are receded by "D").

The following had no connection with the Food & Drug's statement, nor this proposed rule making:

Nine Infants (H1

These subjects were on an experimental efficacy study - under prescription - and had no side effects.

30 Adults (D24)

These subjects were not specific. The reports covers the determination of a controlling dose of vitamin D under prescription for Hypocalcemia.

These two experimental studies cannot be rationally included in the reference to the FDA's statements and intent.

The remaining 113 patients covered in the bibliography fall into four groups:

1) Vitamin D dosage on prescription.
2) Vitamin D dosage on prescription with an additional qualification.
3) Self prescribed.
4) Unknown Origin

) Subjects:

These subjects, together with the previously mentioned 39, were taking vitamin D under prescription and while under the supervision of a doctor (references: H3, D2, H11, H12, D8, D9, H14, D21, H19, D16, D24, D22, H21, D-17, D-27, D18, D29).

One Subject:

This subject had no history of any vitamin D intake whatsoever, but was given a vitamin D loading test and showed no sensitivity (Reference: H27).

One Subject:

This subject instituted vitamin D therapy on his own volition (Reference: H5).

22 Subjects:

These subjects had no known source or specific cause (Reference: H5, H6, H8, D7, H16, D25).

In review: Over a period of 32-years, 152 patients are referred to as being on dosages of vitamin D, ranging from sub-normal to massive, over extensive periods of time. One of these specifically instituted vitamin D dosage of his own volition; 22 are of unknown origin; 113 are on prescription - one was on prescription for a vitamin D loading test. The additional 39 on prescription, as reported are not germane to the question.

It would seem the government's contention is difficult to substantiate in light of these factual figures and statements.

DISCUSSION

From the above, the reported cases of adverse effects claimed with vitamin D, the great preponderance of the subjects were taking vitamin D on prescription and under the supervision of a physician, not of their own volition utilizing over-the-counter products.

The government's statement that daily ingestion, by infants, of doses between 1,000 and 2,000 International Units has produced Hypervitaminosis D, usually manifested as infantile syndrome and other symptoms, is not valid. The condition has manifested itself when vitamin D intake was as low as 400 units (H3) and 800 units (D17). Additionally, the condition has manifested itself with no vitamin D intake (H3, H6, D2, D26).

In specific research, infants and children with infantile Hypercalcemia showed the same D plasmal levels as healthy, normal controls of the same age (H16).

The conditions and symptoms mentioned by the Food & Drug Administration have no specific or confirmed connection with vitamin D and the condition occurring in its absence (H2). The conditions described by the Food & Drug Administration thus appear with or without vitamin D (H4, H6, D2, H11, D7).

The incidence of Infantile Hypercalcemia or Idiopathic Hypercalcemia, as the study of the bibliography shows, is almost non-existent in this country, where the availability of vitamin D - both on the recommendation of a physician and over-the-counter - is widespread.

The government's statement is misleading, since by inference it involved vitamin D as a causative factor when such is not the case; and researchers have stressed the fact that these conditions are probably genetic in origin and not caused by any specific substance. This is attested to by the familial relationship of infantile Hypercalcemia (Reference H14).

The problems encountered in infantile and idiopathic Hypercalcemia are summed up (Reference: H15) by the fact that in infantile or idiopathic Hypercalcemia, usually no large amounts of vitamin D are administered and a genetic error of calcium or vitamin D metabolism is suspect. This reaction can occur with subnormal amounts of vitamin D, calcium and many other substances. The conditions described by the Food & Drug Administration is a disease entity of extremely rare occurrence which manifests itself with no D intake, suboptimal intake and high vitamin D intake, with high calcium intake and other unknown substances. It is genetic in origin, its prevention is not amenable to any vitamin D dosage control. The inference of the Administration, as set forth in their proposal, is therefore misleading.

The remaining cases listed attached deal with the utilization of vitamin D, normally at massive dosages and under prescription, to combat the hypocalcemic effects of hypoparathyroidism and prevent the serious advent of tetany. Just as with diabetics and insulin, the vitamin D is balanced out normally at enormous doses for therapeutic effect in maintaining normal calcium level. These can vary from time-to-time, producing minor hypercalcemia but the patients are always returned to maintenance dosages, which have no adverse effects.

The other primary reports included cover resistant rickets, where again massive doses of vitamin D are utilized to prevent permanent skeletal deformities, and at given maintenance dosages have no adverse or permanent effects.

The incidence of these conditions, which are reported with vitamin D levels ranging from none to 400,000 units, attest to the safety of present dosage forms of vitamin D.

SUMMARY & RECOMMENDATION

The foregoing data demonstrates the lack of potential harm of vitamin D over-the-counter in adult products. Based on the data submitted and previous levels of actual human toxicity (Reference: D30), 10,000 units of vitamin D per unit for adult dosages, would provide a well established safety margin. 1200 International Units of vitamin D per unit dose for infants would provide an equally safe margin of dosage level.

The FDA Vitamin D Bibliography on Teratogenicity listed two animal studies. The remainder, which covered humans, was transferred to the previously discussed human vitamin D.

While, as in the case of vitamin A, animal studies cannot be directly translated into reactions with humans, taking the dosage levels used in the two studies, the proporational level equivalency for a 100 lb. female would be between two-million to four-million units of vitamin D in one study and 37.5-million per day in the other study. Again, a level which couldn't described as massive but more merely approximates the term monsterous.

R. P. Scherer CORPORATION
9425 GRINNELL AVENUE • DETROIT, MICHIGAN 48213 • AREA CODE 313 871-6100

January 29, 1973

TO: Hearing Clerk
Department of Health, Education & Welfare
Room 6-88
5600 Fishers Lane
Rockville, Md. 20852

FROM: Dr. J. P. Stanley

SUBJECT: Vitamin A and Vitamin D Proposed Statement of Policy.
(Fed. Reg. 12-14-72, pp. 26618-26620)
(Correction - Fed. Reg. 1-4-73, p. 799)

Dear Sir:

The R. P. Scherer Corporation, an interested party who will be adversely affected, offers the following comments to the above Proposed Statement of Policy.

The R. P. Scherer Corporation, 9425 Grinnell Avenue, Detroit, Michigan 48213, incorporated under the laws of Delaware, is a major manufacturer of filled soft gelatin capsules which are used primarily as a dosage form for food and drug products. Over fifty percent of such products are vitamin or vitamin-mineral combinations containing the vitamins A and D. These products are manufactured as special or private formulas for many drug companies, both large and small. Besides the private formula type products, the company also manufactures and maintains stock formulas of these products for sale primarily to the smaller houses. All shipments are made in bulk and are properly labeled.

The above Statement of Policy has a direct bearing on approximately 100 products affecting over 300 companies and would adversely affect this company and over 300 customers by requiring the reformulation and/or relabeling of these products. It is the position of the R. P. Scherer Corporation that:

1. The Statement preempts the OTC review of vitamin and mineral products, which panel of experts will be called upon to decide the issue of safety, (as well as efficacy), for products containing higher than dietary supplement vitamin levels. It is probable that additional reformulation and/or labeling will again be required at that time causing a double burden to the industry within a short time period.
2. Neither the Statement nor the bibliography support the need for immediate action based upon the toxicity of these vitamins and current regulations are sufficient to protect the public until the above-mentioned OTC review. See General Comments below.
3. If the Statement is published prior to the OTC review, either as it stands or is changed in accordance with recommendations similar to those of the R. P. Scherer Corporation, appropriate labeling for such products must be supplied by the FDA and sufficient time allowed (greater than the proposed 60 days) for reformulation and/or the relabeling of inventories. See Specific Comments below.

4. Since the Statement concerns itself solely with the issue of toxicity and if the FDA, after reviewing all comments, still feels the need for urgency then a panel of nutritional experts should be called, immediately, to decide this controversial, scientific issue. This approach to the resolution of scientific issues was the recommended procedure proposed by Mr. Peter Hutt in his talk at the FDLI meeting in Washington, D.C., last December.

Further, it is the contention of the R. P. Scherer Corporation:

1. That 25,000 unit (5X RDA) vitamin A products can be supported from a toxicity standpoint and with use of proper labeling can be marketed OTC to adults (i.e., those over 12 years of age).
2. That the same is true for 10,000 unit (ca. 5X RDA) vitamin A products for children 12 years of age and under, including infants.
3. That on the same basis as A, 2,000 unit vitamin D (5X RDA) products can be supported for the OTC adult market.

GENERAL COMMENTS

1. As regards the preamble of the Statement:

   a. Paragraph 1 concerns itself with the OTC availability of vitamin A at 50,000 units (10X RDA) and of vitamin D at 25,000 units (60X RDA). This is essentially correct for vitamin D but currently, all 50,000 unit vitamin A products require the prescription legend per DESI notice 3444, Fed. Reg. 8-19-71. Until this notice, both products were on the market for approximately 20 years labeled as dietary supplements in accordance with the current law and as the result of the Durham-Humphrey amendment.

   b. The next two paragraphs concern themselves with the position of the American Academy of Pediatrics relative to the toxicity of A and D. Actually, the American Academy of Pediatrics presents little or no toxicity data to support their contentions and fears that products containing less than 50,000 units of A or less than 2,000 units of D are actually hazardous to the general health of the public. Nor do they present evidence to support widespread radio, television and lay press advertising which urges the public to take toxic doses of these vitamins. They even state, ".... the incidence of hypervitaminosis A appears to be increasing." Again, no real evidence. Is this a scientific evaluation of the facts and is the FDA forgetting their scientific image in publishing such comments?

c. The bibliography referred to in paragraph 4 does not support the contention of the FDA that products containing between 10,000 and 50,000 units of A and between 400 and 2,000 units of D are sufficiently hazardous to the health of the general public that such products must be on prescription status.

2. As regards the vitamin A position of the Statement:

a. In paragraph 1, it is stated that "doses of 50,000 units in adults and 20,000 units in infants on a daily basis over long periods are known to produce toxicity."

b. If this is true, it is unscientific, as well as illogical, to allow, as in paragraph 4, a 100% safety factor for infants (20,000 I.U. (10X RDA) toxic vs. 10,000 I.U. (ca. 5X RDA) nontoxic) while adults would enjoy a 500% safety factor (50,000 I.U. (10X RDA) toxic vs. 10,000 I.U. (2X RDA) nontoxic). It is agreed that a 100% safety factor is desirable and sufficient to insure consumer safety. Therefore, 25,000 units (5X RDA) for adults would certainly be warranted as a safe OTC product. The FDA bibliography and the literature would support such limits for OTC products.

P. Schorer CORPORATION

Hearing Clerk
Dept. HEW

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3. As regards the vitamin D portion of the Statement:

   a. It is noted that no mention is made as to the toxic level for adults as was done with vitamin A, so it would appear that overdosing of infants is the main concern of the FDA as regards vitamin D toxicity. The FDA bibliography and other literature references support levels of 1,200 units (3X RDA) of D for children to 12 years of age and 2,000 units (5X RDA) of D for adults as not being hazardous to the health of the general public.

SPECIFIC COMMENTS

1. Safety of A and D:

   a. Testimony of nutritional experts at the vitamin hearings support the contention that the ingestion of 3 to 5 times the RDA of any vitamin, including vitamins A and D, poses no toxicity problem or health hazard for the general public. See Olson WD-49, p.3 and WD-46, p.5; Vitale WD-65, pp.9,10 and P.651; Stare WD-49, p.4; Mayer WD-46, pp.20,21; Ershoff WD-60-85, p.3; Grollman Tr.2360, 2361; Harrison Tr.23,230-23,234; and Herbert Tr.14,571-14,575. Thus, this definitely supports an OTC product containing a maximum of 25,000 units of A and/or 2,000 units of D for adults and 10,000 units of A and/or

1,200 units of D for children.

b. Our review also supports the safety of an OTC product containing a maximum of 25,000 units of A for adults and 10,000 units of A for infants and children. My summary of this data indicates 53 references, covering 81 cases over a period of 27 years (1944 thru 1971). The vast majority of cases involve extremely high doses of vitamin A over long periods of time.

c. According to Braun (Pediat. Clin. N. America 9, 935 (1962) the toxicity of vitamin A is self-limiting and recovery is prompt. Since excess consumption of any substance can cause toxic effects, perhaps vitamin A can be related in this respect to readily available, potentially harmful foods such as sugar and salt. The latter household table items are potentially harmful to at least certain segments of the population, much as D might be for certain unusually sensitive individuals, but they are not considered harmful for the general public.

d. More specifically, as regards vitamin D toxicity information, you are referred to a somewhat similar proposal on vitamin D published in the Fed. Reg. of 8-28-65, pp.11140-11141. This proposal was never implemented. It is our

belief that comments filed relative to vitamin D toxicity as the result of that proposal are still appropriate today since there has been no significant new evidence published that would establish a need for immediate action at this time. See specifically the submission of the Wisconsin Alumni Research Foundation dated Dec. 27, 1965 and its attachment "Vitamin D in Nutrition."

e. As in the case of vitamin A, (a. above P.651), the 1968 edition of "Recommended Dietary Allowances" published by the Food and Nutrition Board of the National Academy of Sciences (Publication #1694) does not support the position of the FDA that doses of vitamin D of 2,000 I.U. per day or less are hazardous to the general public. They merely point out that for <u>dietary supplementation</u> it is best to leave the level at 400 I.U. However, it is obvious from their toxicity discussion that properly labeled OTC drug products containing up to 2,000 I.U. of vitamin D would be safe for use by the general public.

2. Labeling (Fed. Reg. 12-14-72, paragraph 10, pg. 26619):

a. The statement does not refer to the exact labeling of vitamin A and D containing products. With the recent publication of the tentative order on dietary supplement

labeling, it will be necessary to develop suitable labeling for current products (intended for 4 years of age and over) containing over 5,000 units of A and over 400 units of D since such products will no longer be labeled as dietary supplements.

b. If the statement stands unchanged, then it should include an FDA acceptable prescription label so that future production of existing products that will become prescription can be properly relabeled.

3. Recommended changes in Statement, ℙ 3._____ Vitamin A preparations for oral use as drugs:

a. No change.

b. In view of ..... in excess of 10,000 I.U. per dosage unit, labeled for use by children up to 12 years of age, or in excess of 25,000 I.U. per dosage unit, labeled for use by those over 12 years of age are drugs subject to ..... sale. Such ..... met:

1. No change.

2. No change (but recommended prescription labeling should be set forth).

c. Preparations containing 10,000 I.U. or less of vitamin A per dosage unit, labeled for use by children up to 12 years of age, or 25,000 I.U. or less of vitamin A per dosage unit, labeled for use by those over 12 years of age, will be ..... exceeds 10,000 I.U. or 25,000 I.U. respectively.

d. Preparations containing over 5,000 I.U. (except approved dietary supplements) but not exceeding 25,000 I.U. of vitamin A per dosage unit are to be labeled as OTC drugs pending the results of the Vitamin-Mineral OTC review. Such products will be regarded as misbranded if the following current label modifications are not met:

1. The label of products containing over 10,000 I.U. of vitamin A per dosage unit or the recommended daily dose is over 10,000 I.U. of A per day must bear a statement "For adults and children over 12 years of age."
2. The label of products containing over 10,000 I.U. of A per dosage unit must bear a warning statement regarding vitamin A toxicity using acceptable wording.
3. To facilitate comparison of products and to fully inform customers, the label of these OTC products must list the name and amount of each vitamin and/or mineral contained therein and the % of the established RDA for each vitamin and/or mineral. The RDAs are standard references for the potency of vitamin products.

e. Vitamin A preparations labeled ..... as of 180 days for prescription products, 1 year for OTC products after day ..... Register.

4. Recommended changes in Statement, ¶ 3._____ Vitamin D preparations for oral use as drugs:

a. No change.

b. In view of ..... in excess of 1,200 I.U. per dosage unit, labeled for use by children up to 12 years of age, or in excess of 2,000 I.U. per dosage unit, labeled for use by those over 12 years of age, are drugs ..... sale. Such ..... met:

1. No change.

2. No change (but recommended prescription labeling should be set forth).

c. Preparations containing 1,200 I.U. or less of vitamin D per dosage unit, labeled for use by children up to 12 years of age, or 2,000 I.U. or less of vitamin D per dosage unit, labeled for use by those over 12 years of age, will be ..... exceeds 1,200 I.U. or 2,000 I.U. respectively.

d. Preparations containing over 400 I.U. but not exceeding 2,000 I.U. of vitamin D per dosage unit are to be labeled as OTC drugs pending the results of the Vitamin-Mineral OTC review. Such products will be regarded as misbranded if the following current label

modifications are not met:

1. The label of products containing over 1,200 I.U. of vitamin D per dosage unit or the recommended daily dose is over 1,200 I.U. of D per day must bear the statement, "For adults and children over 12 years of age."

2. The label of products containing over 400 I.U. of vitamin D per dosage unit must bear a warning statement regarding vitamin D toxicity using acceptable wording.

3. To facilitate comparison of products and to fully inform customers, the label of these OTC products must list the name and amount of each vitamin and/or mineral contained therein and the % of the established RDA for each vitamin and/or mineral. The RDAs are standard references for the potency of vitamin products.

e. Vitamin D preparations labeled ..... as of 180 days for prescription products, 1 year for OTC products, after day ..... Register.

Hearing Clerk
Dept. HEW

The above comments reasonably set forth our position, contentions and recommendations regarding the referenced Statement of Policy. It is requested that the Commissioner give due note and consideration to these comments and defer action on the issue of Vitamin A and Vitamin D toxicity until its proper consideration during the Vitamin and Mineral OTC review. Otherwise, it is requested that the Commissioner revise the Statement of Policy along the lines of the above recommendations.

Respectfully submitted

R. P. SCHERER CORPORATION

J. P. Stanley

J. P. Stanley, Ph.D.
Technical Director

JPS:bk
enc. (References from Vitamin Hearings listed on page 6 of this submission).

LINUS PAULING
PROFESSOR OF CHEMISTRY

Received December 1972

Routing	Action	Info	Comm
GC-1 (Harris Clerk)	✓		
CM-1		✓	
BF-1		✓	

☐ Prepare for Signature of: ☐ Direct Reply

Remarks: No reply necessary

Dr. Charles C. Edwards
Food and Drug Commissioner
Department of Health, Education and Welfare
Food and Drug Administration
Washington, D. C. 20204

Dear Dr. Edwards:

I have read in the newspapers that the Food and Drug Administration is proposing to limit the sale of tablets and capsules without a prescription to those containing not more than 10,000 IU of vitamin A.

I think that such a regulation would be asinine - not quite as asinine as to make a similar limit of 100 mg for vitamin C, as was proposed by the Food and Drug Administration on 9 December 1966, but almost as asinine.

I enclose a statement by me opposing the proposed limitation on the sale of vitamin A, and ask that this statement be included in the evidence, and that I also be invited by you to present oral arguments.

Sincerely,

Linus Pauling

LP:ky
enclosure

Statement on the Proposed FDA Regulation Limiting the Sale of Vitamin A

by Linus Pauling
Professor of Chemistry in Stanford University

I am Linus Pauling, now Professor of Chemistry in Stanford University. I was for 42 years at the California Institute of Technology (for 22 years Chairman of the Division of Chemistry and Chemical Engineering), and have taught in Cornell University, Oxford University, University of California, and other universities. I was born in Portland, Oregon, on 28 February 1901, and educated in the public schools of Condon and Portland, Oregon, in Oregon Agricultural College (B.S. in chemical engineering, 1922), and in the California Institute of Technology (Ph.D. in chemistry, minors in physics and mathematics, 1925).

I received the Nobel Prize for Chemistry in 1954, and have received many other awards in chemistry. I also received the 1962 Nobel Peace Prize in 1963, and have a number of other awards for work for peace and better international relations. I also received the Presidential Medal for Merit, the Naval Ordnance Development Award, and several other awards from the United States Government. I also received the Phillips Medal of the American Academy of Physicians, the Modern Medicine Award, and several other medical awards. I am an honorary member of the Harvard chapter of the medical honor society Alpha Omega Alpha, a corresponding member of the French Academy of Medicine, an honorary member of the American Association of Clinical Chemists, an honorary member of the American Society for Pharmacology and Experimental Therapeutics, honorary president of the Academy of Orthomolecular Psychiatry, and a member of about fifty other scientific and medical societies. I have written about 500 papers and a dozen books on physics, chemistry, medicine, and world affairs.

For 35 years much of my work has been on chemistry in relation to medicine. During recent years I have been especially interested in the possibility of achieving a significant improvement in the health of the American people through improved nutrition, with special reference to the proper role of the vitamins.

COPY

The Proposed Regulation of the Sale of Vitamin A

I am opposed to the proposed limitation of non-prescription sale of vitamin A to tablets and capsules containing not more than 10,000 IU for the following reasons:

1. The optimum daily intake of vitamin A is, in my opinion, about 25,000 IU for many people. The FDA has no convincing evidence that this opinion is not correct. The FDA should not make a regulation that interferes with the proper nutrition of the American people.

2. If the proposed limitation of the sale of vitamin A were extended to foods, a prescription would be required for a serving of one half of one ounce of broiled lamb liver or two ounces of sweet potatoes. The FDA is either wrong in proposing the limitation of the sale of vitamin A tablets on capsules or remiss in not also proposing the equivalent limitation of the sale of liver, sweet potatoes, and other foods rich in vitamin A.

3. There is very little chance of damage to humans from ingesting too much vitamin A - far less chance than for many drugs that are sold over-the-counter. The argument that the proposed regulation would significantly protect the American people from a serious danger, that of hypervitaminosis A, is invalid.

4. The proposed regulation would be largely ineffective, and would be economically damaging to the public.

5. The proposed action would, without justification, limit the freedom of the people.

The Optimum Intake of Vitamin A

The optimum intake of a vitamin is the intake that leads to the best of health. This optimum intake is probably different for different persons. The average value of the optimum intake of vitamin A for an adult is not known. I estimate it to be about 25,000 IU per day.

Some evidence to support this value is provided by the work of H. C. Sherman and H. Y. Trupp with rats, Proc. Nat. Acad. Sci. USA 35, 90 (1949). Additional evidence is provided by the consideration of the average amount in a day's ration of 110 raw natural plant foods, in the same way as described for vitamin C in my paper Evolution and the Need for Ascorbic Acid, Proc. Nat. Acad. Sci. USA 67, 1643 (1970), and my book Vitamin C and the Common Cold, 1970. This average for vitamin A is 110,000 IU. When the 16 plant foods with the highest values, above 200,000 in a day's ration, are omitted, the average for the other 94 is 29,000 IU. Even with consideration of the contribution of meat to the diet, there is strong indication that primitive man ingested much more than 10,000 IU of vitamin A per day.

Further evidence that the optimum intake of vitamin A is larger than 10,000 IU per day is that the "therapeutic dose" prescribed by many physicians to improve the health of some patients is usually 25,000 or 50,000 IU per day.

That the optimum intake of a vitamin may be considerably greater than the amount needed to prevent overt avitaminosis or the "recommended daily allowance," which is usually two to five times greater, is shown by the effectiveness of ascorbic acid in amounts 20 to 100 times the "recommended daily allowance" in providing protection against the common cold. The older evidence is summarized in my book Vitamin C and the Common Cold. The new evidence reported by Charleston and Clegg, Lancet 1, 1401 (1972), and by Anderson, Reid,

and Beaton, J. Canadian Med. Assn. 107, 503 (1972), leaves little basis for skepticism.

The Food and Drug Administration, in justice to the American people, could ethically restrict the non-prescription sale to tablets or capsules containing no more than 10,000 IU of vitamin A only if the FDA had convincing scientific evidence that the optimum daily intake for most people, leading to the best of health, were less than 10,000 IU. The Administration does not have such evidence. In fact, the existing evidence indicates that the optimum daily intake is greater than 10,000 IU. It would accordingly be wrong for the FDA to limit the sale of vitamin A in this way.

COPY

Why Should the Sale of Tablets be Restricted and Not That of Foods?

It is proposed that the non-prescription sale of tablets or capsules containing more than 10,000 IU of vitamin A be forbidden, but not that of portions of foods containing more than 10,000 IU of vitamin A.

Either the FDA is wrong in forbidding the sale of the tablets, or it is remiss in not forbidding the sale of a portion of certain foods.

Occasionally I eat a serving of one half pound of liver. According to the book Metabolism of the Federation of American Societies for Experimental Biology, a one half pound portion of raw beef liver contains 100,000 IU of vitamin A, of fried beef liver 121,000 IU, of raw lamb liver 115,000 IU, and of broiled lamb liver 169,000 IU. To be consistent, the FDA should propose restricting the sale by butcher shops and restaurants of beef or lamb in portions greater than half of one ounce (for broiled lamb liver) and 0.8 ounce (for raw beef liver), except when prescribed by a physician.

I also occasionally eat a half pound serving of sweet potatoes. According to the book Metabolism, this serving contains between 18,000 and 45,000 IU of vitamin A. To be consistent, the FDA should restrict the non-prescription sale of sweet potatoes to about two ounces per portion.

There is Little Danger of Hypervitaminosis A

A reason given for restricting the sale of vitamin A is that very large amounts are damaging to the health of human beings.

In fact, there is very little danger of damage through hypervitaminosis A, whereas much damage (ulcers, deaths) is done by aspirin and other drugs that are sold over-the-counter.

So far as I am aware, no person has been killed by taking too many tablets or capsules of vitamin A.

An intake by an adult of 200,000 IU of vitamin A over a period of a year or more has caused some cases of hypervitaminosis A. A somewhat smaller intake, down to about 100,000 IU per day, has caused hypervitaminosis A in infants. A single dose of several million IU causes illness. The disease is brought under control in a few days by decreasing the intake of the vitamin.

Many people have ingested 50,000 to 100,000 IU per day (by eating one half to one pound of liver per day, for example) over long periods of time, without developing hypervitaminosis A.

The facts show that the danger of hypervitaminosis A is not great enough to justify the proposed restriction on the sale of this vitamin.

The Proposed Regulation Would be Largely Ineffective but Would be Economically Damaging to the Public

It is customary now for people who recognize improvement in their health with increased intake of vitamin A to purchase capsules containing 25,000 IU, at a retail price of about $5.00 for a year's supply (365 capsules).

If these capsules could not be obtained, many people probably would take five 5,000 IU capsules per day. The regulation would be ineffective, but it would have some nuisance value in discouraging some people from improving their health by reaching the optimum intake of this vitamin.

Inspection of price lists shows that the cost per unit of vitamin capsules containing 5000 or 10,000 IU is two or three times that of capsules containing 25,000 IU. Accordingly the proposed regulation, if put into effect, would mean for many people only an unnecessary extra cost of $5.00 or $10.00 per year paid for this important nutrient.

A fraction (rather small) of the American people might rely upon their physicians to prescribe vitamin A for them. They also would suffer financially, in having to pay the physician for writing the prescription and in having to pay the customary overcharge for prescriptions as compared with over-the-counter items.

The Proposed Action Would Limit the Freedom of the People

The proposed restriction on the sale of vitamin A would, if it went into effect, limit the freedom of the American people, with no discernible advantage to the country or the government, and with disadvantage to the people themselves. It probably would lead to a black market in vitamin A capsules, and to the increase in crime that is associated with the development of a black market. The Volstead Act, which limited the sale of alcoholic liquors except on a physician's prescription, had some justification, but it failed. The proposed limitation of the sale of vitamin A has no justification.

For the reasons given above, this proposed regulation should be rejected.

Linus Pauling

COPY

Department of Health, Education and Welfare
Room 6-88
5600 Fishers Lane
Rockville, Md. 20852

Comments concerning proposed policy statement concerning Vitamin A and vitamin D.

Although an employee of the Food and Drug Administration, Division of Nutrition for over twenty two years I have been informed that there is no reason that I cannot respond as an interested party.

Several years of my professional life with FDA was spent as an analyst, both biological and chemical, of the vitamins A and D. Also I have spent some time with research involving actions of both vitamins and as a result of this work and a literature search performed for the part 125, Special Dietary Food Hearings, I am reasonably acquainted with the scientific literature involving these two vitamins.

My objection is not to the general need to limit the availability of products that will supply truly dangerous amounts of them but to the levels chosen. In truth, the only thing that the proposed policy will accomplish is a form of harassment to the individuals who choose to take high levels of either. This may be somewhat effective in that it doubles or quadruples the number of pills but usually for these individuals the quantity is no deterant however it does increase the cost.

I have no strong objection to the 10,000 unit limit for vitamin A but since this level or even a somewhat higher level is not really dangerous I feel that a prescription requirement is rather capricious and highly subjective. I would suggest that potencies between 8,000 (the allowance for pregnancy) and 15,000 be designated as OTC drugs. Since this would be beyond the allowable potency for a dietary supplement and below a potency required for therapeutic use, this range is effectively eliminated since adequate directions for use cannot be written unless future research demonstrates an effective therapeutic use in this range. For the sake of uniformity the Canadian floor of 10,000 could be used for the OTC range but the supplement level should then be raised to this level, at least for use in products intended for use in pregnancy and lactation, since there really are no demonstrated hazards up to this level. Products for adult use could be properly and reasonably limited to 7,500 units, 150% of the adult RDA.

The 400 unit limit for vitamin D is most unreasonable, ill conceived and irrational. This tight limit at the RDA implies a very narrow and critical

limit for toxicity which is not true. I agree that there are no normal circumstances when consumption of more than the 400 units is of value, especially for the adult, but the available information does not justify as reasonable the establishment of a requirement of a prescription for this level. It is most irrational because, as a matter of fact, because of analytical difficulties and manufacturing practices, there is not a 400 unit product on the market that does not actually contain an excess which in spite of labeling would catagorize it as a prescription product. In addition, many natural sources of A and D contain them in a ratio of 10:1 which would force manufacturers using them to underclare the vitamin D in order to comply with the limit. This would be contrary to the purpose of the policy and in addition results in an FDA inforced mislabeling which is most certainly contrary to the intent of the whole FD & C law. It has also come to my attention that some purveyors of natural vitamin A simply do not label any vitamin D, probably because of the difficulty and expence of the assay and quality control but it may also be deliberate because of a rather general feeling on the part of potential consumers that excess vitamin D is not desirable. This whole area is inconsistant with the false but implied danger of vitamin D levels above 400 units in this proposal. I would suggest adoption of the Canadian 1,000 unit limit with the range between 600 (150% of the RDA) and 1,000 units as OTC. Difficulties with "directions for use", as for vitamin A, would also apply to this range.

Sincerely yours,

Glen M. Shue

Glen M. Shue
Technical Assistant
Division of Nutrition
Food and Drug Administration

17 January 1973

AMERICAN MEDICAL ASSOCIATION
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COUNCIL ON
FOODS AND NUTRITION
Office of the Secretary

February 13, 1973

Miss Beryl McCullar
Hearing Clerk
Department of Health, Education,
and Welfare
Room 6-88
5600 Fishers Lane
Rockville, Maryland 20852

Dear Miss McCullar:

The Council on Foods and Nutrition has reviewed the Proposed Statement of Policy on Vitamin A and Vitamin D published in the Federal Register of December 14, 1972 (37CFR 26618).

The Council endorses the proposal to restrict the amounts of vitamin A and vitamin D in over-the-counter preparations.

Evidence for the restriction of vitamin D beyond that given in the preamble to the proposed amendment, may be found in a paper by Alan I. Fleischman, et al, "Vitamin D and Hypercholesterolemia in Adult Humans," pp. 468-472 in "Atherosclerosis: Proceedings of the Second International Symposium"; Springer-Verlag, New York-Heidelberg-Berlin, 1970. The studies reported significant increase in plasma cholesterol with the ingestion of 1,000 IU vitamin D daily.

The Council also notes that the discussion of the NAS/NRC RDA in the December 14 proposal fails to mention that there is no RDA for vitamin D in the case of adults. Requirements are presumably met by ordinary mixed diets and exposure of the skin to sunlight.

The Council assumes that the establishment of finite upper limits for vitamins A and D, would not preclude controlled "overage" to assure compliance with label declarations of the amounts present.

The maximum amount of vitamin A, 10,000 IU, that would be permitted by the present proposal is greater than the maximum permitted in the proposal published in the January 19, 1973 Federal Register, namely 5,000 IU for adults and 8,000 IU for pregnant or lactating women (38CFR2161-2162).

Recognizing that the present proposal is of an interim nature to place limits on over-the-counter preparations, the Council endorses the upper limit of 10,000 IU of vitamin A. The Council on Foods and Nutrition will comment at a later date on the proposals of January 19, 1973.

Sincerely,

Philip L. White

Philip L. White, Sc.D.
Secretary

PLW:vm
enclosures: 4 copies of this letter of February 13, 1973

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February 15, 1973

Miss Beryl McCullar, Hearing Clerk
Department of Health, Education
and Welfare
Room 6-62
5600 Fishers Lane
Rockville, Maryland 20852

Dear Miss McCullar:

The Committee on Nutrition of the American Academy of Pediatrics, which has been active in nutritional matter for over 15 years, wishes to comment on the proposed regulations concerning Vitamin A & D which appeared in the Federal Register, Vol. 37, No. 241, December 14, 1972, pages 26618-26620.

The Committee on Nutrition recommends that Vitamin D in amounts up to 1000 I..U. be allowed without prescription in foods for special dietary use for specific medical problems - in this instance foods, designed for dietary management of subjects with poor Vitamin D absorption and steatorrhea or fat malabsorption.

Considerable evidence exists that there is Vitamin D deficiency leading to osteomalacia associated with steatorrhea. Providing Vitamin D in amounts up to 1000 I.U. for daily consumption in foods designed for patients with steatorrhea will provide some protection from Vitamin D deficiency and entails no risk of Vitamin D excess. This exception is requested only for special foods and not for vitamin and mineral supplements because the latter may be used in excess, whereas the foods cannot be taken in great excess.

This exception will permit continued use of established recommended dietary regimens for steatorrhea. Your consideration of this proposal will be appreciated.

Very sincerely yours,

Malcolm A. Holliday

Malcolm A. Holliday, M.D.
Chairman, Committee on Nutrition
American Academy of Pediatrics

MAH:vs

Oklahoma State University
Department of Food, Nutrition and Institution Administration
STILLWATER, OKLAHOMA 74074
(405) 372-6211, Exts. 6007, 6091

April 16, 1973

Federal Register
Hearing Clerk
Department of Health, Education, and Welfare
Food and Drug Administration
Washington, D.C. 20000

The Oklahoma Nutrition Task Force wishes to state that we are in accord with the proposal to limit the strength of Vitamin A adn D products available for over-the-counter sale. The proposed daily limit of 10,000 I.U. for Vitamin A and 400 I.U. for Vitamin D is at a level assumed to be within safe limits. Evidence of fat soluble vitamin toxicities has been established and high dosages pose health hazards.

We concur that these products should be regulated for consumer protection as long as non-prescription vitamin supplements are freely available.

Esther Winterfeldt

Esther Winterfeldt, Ph.D.
Chairman
Oklahoma Nutrition Task Force

EW:bw

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196a

January 22, 1973

Miss Beryl McCullar, Hearing Clerk
Department of Health, Education and Welfare
Room 6-62
5600 Fishers Lane
Rockville, Maryland 20852

Dear Miss McCullar:

1. I fully support the proposal (FDA, December 14, 1972) requiring all preparations providing daily dosage of more than 10,000 I. U. vitamin A or 400 I. U. vitamin D to be sold by prescription only.

2. The objections raised by pharmaceutical houses are based on the argument that this regulation will inconvenience certain patients with malabsorption and will stifle development of special foods. Both arguments are fallacious.

The drug houses have long used "special needs" as a front for promoting useless and dangerous nutrient remedies, e.g. artificial sweeteners, a nonsensical aid for diabetics, was promoted into a national industry.

Persons with special dietary needs would be better served by prescription nutrients. Indeed, I think all vitamin preparations should be put on prescription requirement, and I think this will happen in time. The A/D requirement is a good beginning. In my opinion, a maximum of 5,000 I. U. for vitamin A would have been more judicious. I hope that the OTC Drug Advisory Review Panel will consider this proposal.

Sincerely yours,

George Mann

George V. Mann, M.D.
Vanderbilt University

GVM:jv

The United Liverpool Hospitals

197a

Department of Chemical Pathology, Ashton Street, Liverpool L3 5RT.

Telephone: 051-709 2085

If telephoning, please ask for

Your ref:

Our ref: WHT/JIC

2nd January, 1973

The Hearing Clerk,
Department of Health, Education and Welfare,
Rm. 6-86,
5600 Fisher's Lane,
Rockville, Maryland 20852,
U.S.A.

Dear Sir,

I understand from Dr. J. Yogamundi Moon that the Food and Drug Administration is, at present, considering a proposal to make all preparations containing over 400 I.U. of vitamin D available only on a prescription. Dr. Moon has suggested that I might send to you a copy of my recent paper on the relationship between renal calculi and self-medication with multivitamin preparations. I have pleasure in enclosing this paper.

Since the publication of this paper we have accumulated further evidence, as yet unpublished, that the continued administration of amounts of vitamin D of the order of 500 to 1,500 I.U. daily over several months promotes a hypercalciuria in a proportion of subjects. We have also found from studies of dietary history that very few normal, healthy adults take, or appear to need, more than 200 I.U. of vitamin D daily and the mean value is closer to 100 I.U. daily.

From these facts, and from those already published in the enclosed paper, I would like to suggest to the F.D.A. that:

1. All preparations should contain an exact amount of vitamin D and not, as is so often the case, a minimal amount. This latter practice may lead to very considerably more vitamin D being taken than is intended.

2. The preparations containing vitamin D should be of two sorts:

    a. Those which can be purchased from pharmacists without prescriptions. For these I recommend that each tablet or capsule should contain 100 I.U. of vitamin D, and that the recommended dose should not exceed one tablet or capsule daily.

b. Preparations containing greater than 100 I.U. per tablet or capsule should be available only on a prescription and should be used for the treatment of established deficiency disorders, such as malabsorption, senile osteomalacia and so forth.

I would regard 100 I.U. daily (as in 2a.) as being a perfectly adequate supplement for any normal adult. I would regard the safety margin as being slight, so that 400 I.U. daily, if combined with a diet rich in foods containing natural or added vitamin D, could place a normal adult at risk of hypercalciuria and then of renal stone formation.

I would be very pleased to discuss this matter more fully if anybody in the organisation would wish me to do so.

I hope that my writing to you in this way is in order; it is not in any way intended to be presumptuous.

Yours faithfully,

W. H. Taylor

W. H. Taylor, M.A., B.Ch., D.M.(Oxon).
F.R.C.P.
Consultant Chemical Pathologist,
Director of Studies in Chemical Pathology,
University of Liverpool.

Clinical Science (1972) 42, 515–522.

RENAL CALCULI AND SELF-MEDICATION WITH MULTIVITAMIN PREPARATIONS CONTAINING VITAMIN D

W. H. TAYLOR

Department of Chemical Pathology, The United Liverpool Hospitals

(*Received* 10 *December* 1971)

SUMMARY

1. Of 104 patients with renal calculi, 42% gave a history of previous self-medication with multivitamin preparations containing vitamin D, compared with 37% of a control group of fifty-one patients without renal calculi. This difference is not significant.

2. The mean supplemental daily intake of vitamin D and the annual intake were significantly higher in the patients with renal calculi than in the control group.

3. The highest mean supplemental intake of vitamin D occurred among those patients in whom no metabolic or other cause for renal stone formation could be found.

4. The first calculi presented within 2 years of the period of self-medication in twenty-four of thirty patients who had not previously suffered from renal stones.

5. The results suggest that self-administration of vitamin D should be included among the aetiological factors promoting the formation of renal calculi.

Key words: renal calculi, vitamin D, self medication.

In about one-third of the patients who are investigated for renal calculi, no metabolic or other cause can be found (Table 1), despite an exhaustive search for the known aetiological factors. The management of this group of patients is thus unsatisfactory, for without a known cause rational therapy is difficult.

A possible clue to the origin of renal calculi in some of these patients emerged while recording their dietary habits and supplemental vitamin D intake. It was observed that self-administration of vitamin D was quite common. The question is thus raised whether such self-administration makes a significant aetiological contribution to stone formation in this group of patients, and whether it perhaps aggravates the formation of calculi in other patients who have a known metabolic cause, such as idiopathic hypercalciuria.

The first step in investigating these possibilities seemed to be a statistical enquiry, the

Correspondence: Dr W. H. Taylor, Department of Chemical Pathology, Ashton Street, Liverpool L3 5RT.

results of which suggest that vitamin D should now be included among the aetiological factors promoting the formation of renal calculi.

PATIENTS AND METHODS

The supplemental vitamin D intake of patients with renal calculi arising from different causes has been compared with that of a continuous series of fifty-one outpatients suffering from metabolic disorders without renal calculi (Table 1). The group with 'other metabolic causes'

TABLE 1. Self-administration of supplemental vitamin D in 104 patients with renal calculi compared with fifty-one out-patients with metabolic disease but without renal calculi

	No. of patients	Self-administration of preparations containing vitamin D, within previous:									
		16 years		10 years		5 years		2 years		1 year	
		No.	%	No.	%	No.	%	No.	%	No.	%
Patients without renal calculi	51	19	37	16	31	12	24	10	20	7	14
Patients with renal calculi associated with:											
Idiopathic hypercalciuria	46	18	39	17	37	13	28	10	22	9	20
Chronic urinary tract infection	12	6	50	6	50	4	33	4	33	3	25
Other metabolic causes	14	6	43	3	21	2	14	2	14	2	14
No known cause	32	14	44	14	44	13	41	7	22	5	16
Total	104	44	42	40	38	32	31	23	22	19	18

comprised six patients with idiopathic phosphaturia, seven with urate calculi and increased serum urate concentrations, and one with hyperoxaluria. The group with 'no known cause' consisted of patients in whom infection, primary hyperparathyroidism, idiopathic or other hypercalciuria, cystinuria, and the metabolic causes mentioned above had been excluded on one or more occasions. The age and sex composition of the groups of patients with and without renal calculi did not differ significantly.

The supplemental intake of vitamin D in the control patients and in all but four of those with renal calculi was ascertained by the same observer. The patients with renal calculi were referred from medical sources with either a confirmed diagnosis or with a history of apparent renal colic. The diagnosis was known at the first interview in only 38% of the control group. In both groups the information about vitamin D intake was obtained by using the same careful pattern of questioning, which came immediately after questions about the dietary history. The patient was asked if he or she had ever taken medicines for indigestion and, if so, their names; the possible intake of sodium bicarbonate was then specifically mentioned. The patient was next asked if at any period of his life he had taken other medicines or tablets obtained from pharmacists, and then, in particular, any containing extra vitamins. If the answer was

no, the patient was asked if vitamin tablets had ever been supplied by his employer(s), and if, specifically, he had ever taken vitamin D. If the answer was still no, the names of the most commonly used vitamin supplements were mentioned.

When the answer was yes, an attempt was made to establish the years of intake, the daily dosage and the duration of each period of continuous administration. It was possible to establish the years of intake by relating self-administration to specific events in the patient's life, and particularly to the onset of illness.

It was surprising to find that some patients gave quite clear and precise descriptions of supplemental vitamin D intake between 10 and 16 years previously. Because renal calculi may remain undetected for several years it was felt that such descriptions had relevance, despite any loss of accuracy caused by the passage of time, and they have therefore been included in the Tables.

The daily dosage was established by detailed questioning, particularly about the times of day at which the supplements were usually taken, and verified whenever possible by independent questioning of husbands or wives. The duration of continuous administration was cross-checked by asking how frequently bottles of tablets or capsules were purchased, and by ascertaining how many tablets or capsules were dispensed in each pack. The brand of supplement was checked by asking patients to describe the size, colour and shape. Finally the quantitative amounts of supplemental vitamin D were calculated from the vitamin D content of the tablets or capsules as quoted in the appropriate edition of the Extra Pharmacopoeia. No quantitative assessment of the information obtained in this enquiry was made, nor were any calculations made, until the enquiry had been completed.

RESULTS

Table 1 shows that the proportion of patients with renal calculi who said they had taken supplemental vitamin D, other than from their own doctor, at any time during the previous 16 years was greater than in the control group, but the differences are not significant. Vitamin supplements taken during childhood are excluded from the results.

Table 2 shows, however, that the mean additional daily intake of vitamin D during the period of supplementation was higher than in the control group in all but one of the groups with renal calculi. The mean intake for all the patients with renal calculi ($0{\cdot}04<P<0{\cdot}05$) and that for the group with 'no known cause' ($0{\cdot}02<P<0{\cdot}03$) both differed significantly from the mean intake of the control group. In other individual groups the difference was not statistically significant. It was also possible in most patients to assess the quantity of vitamin D taken in a year and Table 2 shows that significantly more patients with renal calculi ingested over 100 000 i.u. than in the control group ($P<0{\cdot}02$). The highest daily intake was 3600 i.u. and the highest yearly intake, 550 000 i.u.; both patients were in the group with 'no known cause' for their renal calculi.

Of the nineteen control patients who took supplementary vitamin D only five (26·3%) did so for more than 1 year. In contrast with this ten (55·6%) of eighteen patients with idiopathic hypercalciuria took vitamin D for more than 1 year, as did eighteen (41%) out of the total of forty-four patients with renal calculi. These differences are not statistically significant.

The time relationship between the appearance of the first renal calculus and the first

TABLE 2. Intake of vitamin D in those patients with renal calculi who had taken supplemental vitamin D, compared with that of patients without renal calculi

	Mean daily supplemental dosage (i.u.)	Daily supplemental vitamin D intake of individual patients (i.u.)						Supplemental intake of vitamin D in individual patients during 1 year	
		1–400	401–800	801–1200	1201–1600	1601–2000	>2000	Below 100 000 i.u.	Above 100 000 i.u.
Patients without renal calculi	691	8	7	2	0	2	0	16	3
Patients with renal calculi	982								
Those with:									
Idiopathic hypercalciuria	934	2	8	6	0	2	0	9	8
Chronic urinary tract infection	862	2	3	0	0	1	0	4	2
Other metabolic causes	630	2	3	1	0	0	0	3	3
No known cause	1254	3	5	2	1	2	1	6	8
Total		9	19	9	1	5	1	22	21

supplemental vitamin D is shown in Table 3. In fourteen patients the first renal calculus preceded the taking of vitamin D supplements, but within 2 years of taking the supplements six of these patients experienced further formation of renal calculi. In twenty-four patients the first evidence of renal calculus formation followed within 2 years of ingesting the additional vitamin D. In some patients there was more than one such related episode. For example, a 45-year-old male took 1650 i.u. of vitamin D daily, with a total dosage of 148 500 i.u. in 1962. His first renal calculus was passed in 1963. In 1964 and again in 1965 he took 1100 i.u.

TABLE 3. Appearance of symptoms or signs of renal calculi in relation to supplemental vitamin D intake

Patients with renal calculi associated with:	Calculi preceded supplements	Supplements preceded calculi by:		
		1 year	2 years	>2 years
Idiopathic hypercalciuria	8	6	3	1
Chronic urinary tract infection	0	3	2	1
Other metabolic causes	1	1	1	3
No known cause	5	6	2	1
Total	14	16	8	6

daily for 1 month. Two new renal calculi were passed in 1966. If the intake of supplemental vitamin D were completely unrelated to the formation of renal calculi, it would be expected that the time-intervals between the two events would be more widely dispersed than was found (Table 3).

The proportion of patients whose stones developed after vitamin D ingestion (thirty of forty-four) is in fact significantly greater ($P<0{\cdot}05$) than that of patients who took vitamin D after first developing renal calculi (fourteen of forty-four). The assumption behind such a calculation would be that if the intake of vitamin D and the formation of renal calculi were unrelated, there would be equal chances of either event preceding the other in the patients who experienced both. It is impossible to prove or disprove such an assumption, so that the statistical difference is not one upon which reliance should be placed.

Patients and controls usually obtained their supplements by direct purchase from pharmacists. In only five instances were the preparations supplied by employers. Two preparations that have been particularly promoted by advertisement were consumed by about half of the patients and controls, thirty-one out of a total of sixty-three. These preparations are unfortunately among those which have the highest content of vitamin D per tablet or capsule; in both the quantity exceeds 500 i.u.

DISCUSSION

Patients' recollections of past events are notoriously subject to error. This error can be minimized, as in the present study, by adopting a standard manner of questioning, and by questioning a control group of patients in an identical fashion. The patients presented in such a way that the diagnosis of renal calculus was known or could be inferred. The metabolic

cause of the renal calculi was, however, not known in any patient at the time of questioning. Whereas possible subconscious bias cannot be fully eliminated, it is apparent from Table 2 that bias in questioning did not arise within, for example, the groups with 'other metabolic causes' or 'chronic urinary tract infection'. These results suggest that significant overall bias is unlikely to have occurred. Another possible source of error is that the tablets or capsules taken by the patients may not have contained the precise amounts of calciferol that are stated in the Extra Pharmacopoeia. This potential error is, however, approximately the same for the patients and the controls, for of the three most commonly used supplements, one was used by 20% of patients and 30% of controls, a second by 33% of patients and 20% of controls and a third by 18% of patients and 30% of controls. Thus three preparations accounted for 71% and 80% respectively of the supplements that were taken.

Although the questioning did not reveal any increasing uncertainty about vitamin D intake with passage of time, it is only reasonable to imagine that information recalled after, say, 10 years might not be very accurate. The bearing of these values on the observed differences can be assessed as follows. Three control patients gave information relating to the 10–16 year period and reported that their daily intakes were 250, 550 and 1800 i.u. If they were to be excluded, the control group mean and range would both be decreased. Four patients with renal calculi also gave information relating to the same period and reported daily intakes of 250, 550, 600 and 750 i.u. Since all these values are below the mean daily intake of this group (Table 2), their exclusion would raise the mean. Thus excluding all seven patients would enhance the significance of the difference (P now 0·03–0·04) between the respective means.

It was unexpected that as many as 37% of the patients without renal calculi were found to have taken vitamin D containing supplements, at their own expense, at some point within the previous 16 years. Questioning revealed that a few had undoubtedly been influenced by the various prophylactic claims made for the supplements, but many had felt generally unwell before their metabolic illness had become sufficiently severe to cause them to consult their family doctor, and they had hopefully tried, for a short time, the effect of a vitamin supplement at this early stage.

By contrast, the patients with renal calculi did not, in general, begin to take supplemental vitamins because they were feeling ill, as did the typical control patient, but because they wished to maintain a state of positive health and particularly to prevent winter colds. They thus took the vitamin supplements more regularly and often for longer periods. Those who considered the supplements to be effective naturally took them in subsequent years and sometimes in increased doses.

The differences between the control patients and those with renal calculi all point in the same direction, but only three have statistical significance. The mean daily supplemental intake of vitamin D was significantly higher in the patients with renal calculi than in the control group, and so was the ascertainable annual intake. The mean daily intake of the patients with 'no known cause' for the renal calculi was also significantly higher than that of the control group.

The question therefore arises as to whether the vitamin D supplements have contributed to the formation of renal calculi. Clearly the majority (58%) of patients with renal calculi had not taken extra vitamin D. On the other hand, the presentation of the disease in twenty-four of thirty patients within 2 years of taking the supplements points to the probability that the supplements were a contributing or precipitating factor, as does the fact that of the

fourteen patients who were known to have had renal calculi before ingesting vitamin D, six suffered further renal calculi within 2 years of the supplementation.

One possible mechanism by which the supplements could affect renal stone formation would be by increasing the absorption of dietary calcium and in turn the urinary excretion of calcium. It is, however, not certain that the amounts of vitamin D involved would promote a significant hypercalciuria. The experimental observations on this point are scanty and equivocal. McCance & Widdowson (1942) gave 2000 i.u. of vitamin D daily for 21 days to four normal men and four normal women. They found no increase of urinary calcium output and were thus in agreement with previous observations, which they cited, but of which they were justifiably critical. Their studies are not precisely related to ours, because our patients took their vitamin supplements for a longer time. It is curious, too, that in their eight subjects the daily urinary calcium output ranged from 27 to 179 mg, with five values of 100 mg or less. In contemporary practice, values below 100 mg would be considered low and worthy of further investigation. Flocks (1940) found that, 'in ordinary therapeutic dose in the normal individual, vitamin D raises the urinary calcium not more than 50 mg per 24 hours'. Unfortunately the dosage of vitamin D and the time for which it was given are not stated. He makes the further interesting observation that, 'individuals with so-called "idiopathic" increased urinary calcium show marked response to vitamin D intake', and quotes a range for urinary calcium of 300–500 mg daily, that increases with vitamin D administration (amount not stated) to 500–750 mg daily. Knapp (1947) gave boys aged 1–12 years 340 i.u. of vitamin D daily and found an increased urinary calcium output, but this did not happen in girls treated similarly.

Ideally one would like to know just how sensitive the urinary calcium output is to long-term supplements of vitamin D in patients with renal calculi and in controls, but in the former group at any rate, in the light of the evidence presented in Tables 1–3, such an investigation would scarcely be ethically justifiable. The writer has, however, observed personally that many patients who absorb calcium poorly (for a variety of reasons) and who have been maintained for some weeks in neutral balance on supplements of vitamin D of the order of 500–3000 i.u. daily, often develop hypercalciuria and then require a reduction in their maintenance dose. It would thus not be incompatible with the available evidence to postulate that long-continued supplementary vitamin D in patients without malabsorption eventually increases the absorption of calcium to a point that promotes a hypercalciuria, which in turn would favour increased deposition of calcium in the kidneys. Clearly, patients who normally have above normal calcium intakes would be especially at risk, as would patients who already have idiopathic hypercalciuria [particularly if, as Flocks (1940) suggests, they are unduly sensitive to vitamin D] or some other cause of renal stone formation.

An unexpected finding of this investigation has been the previous relatively high intake of vitamin D in many of the patients with 'no known cause' for their renal calculi. If this supplementation has contributed to the formation of renal calculi, then the group of subjects with 'no known cause' has been decreased further, so that a group of only about 20% remains without even a partial explanation of their renal calculi.

The preparations that were taken also contained vitamin A, except for one, which was taken by one patient in each of the two groups. Similar differences between the groups are likely therefore to exist for vitamin A intake as for vitamin D, but from the known actions of the two vitamins, it seems more probable that formation of renal calculi is related to the latter than to the former. Other vitamins were contained in the preparations taken in 70%

of the control patients and in 57% of those with renal calculi. Similar differences between the groups are thus less likely than with vitamin A, and again the actions of other vitamins are not known to be related to renal stone formation. Two of the control patients had taken medicaments containing small amounts of calcium, as had three of the patients with renal calculi. These supplements are unlikely to affect the validity of the conclusions.

If it is accepted that there is an association between self-supplementation with vitamin D and the formation of renal calculi, the amounts of vitamin D in multivitamin preparations may need to be modified. In the report of the Department of Health and Social Security (1969) it is said of vitamin D that 'of the requirements of adults, including the elderly, practically nothing is known', and a daily adult intake of 100 i.u. is recommended 'as a safety measure'. Over the last two decades there has been a general recognition that in groups thought to be particularly vulnerable to vitamin D deficiency, such as young children, pregnant women and lactating mothers, the recommended intake of vitamin D should be decreased (Department of Health and Social Security, 1969). A reappraisal of adult supplements may therefore be appropriate. Of twenty-six proprietary multivitamin tablets or capsules listed in the Extra Pharmacopoeia (1967), only three contain less than 300 i.u. whereas fourteen contain 500 i.u. or more and three contain 1000 i.u. If patients are able to obtain multivitamin supplements without prescription there seems to be no good reason for a tablet or capsule to contain more than the recommended daily adult intake.

Therefore the following are suggested. (a) Patients who have suffered from renal calculi should avoid self-medication with vitamin supplements containing vitamin D. (b) When vitamin tablets are prescribed for patients who are eating food normally and who do not suffer from malabsorption, the daily supplemental intake of vitamin D should not exceed the recommended daily adult intake. (c) A distinction should be made, with respect to the content of vitamin D, between multivitamin preparations that are meant to be used to maintain an optimum normal intake of nutrients and those that are intended to combat deficiencies, as in the various malabsorption syndromes. It would be desirable for the latter preparations to be available only on medical prescription.

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Mr. McCORMACK. Mr. Speaker, I ve the previous question on the mo- to recommit.

The previous question was ordered.

The SPEAKER. The question is on motion to recommit.

Mr. MILLER of Nebraska. Mr. aker, on that I demand the yeas and s.

The yeas and nays were refused.

Mr. MILLER of Nebraska. Mr. aker, a parliamentary inquiry. I be- the majority leader asked for the and nays on the previous question. sire to have a vote on the passage he bill and on the motion to recom- Is it in order to ask for tellers on vote on the passage of the bill?

The SPEAKER. We have not reached point yet.

The question is on the motion to re- mit.

Mr. MILLER of Nebraska. On that I for tellers, Mr. Speaker.

Tellers were ordered, and the Speaker pointed as tellers Mr. McMILLAN and MILLER of Nebraska.

The question was taken; and the tel- reported that there were—ayes 103, s 153.

So the motion to recommit was re- ted.

The SPEAKER. The question is on passage of the bill.

Mr. ABERNETHY. Mr. Speaker, on t I ask for the yeas and nays.

The yeas and nays were refused.

The bill was passed.

A motion to reconsider was laid on table.

AUTHORIZING SALE OF CERTAIN AL- OTTED LAND ON THE BLACKFEET ESERVATION, MONT.

Mr. MORRIS. Mr. Speaker, I ask nanimous consent to take from the aker's desk the bill (H. R. 629) to horize the sale of certain allotted on the Blackfeet Reservation, nt., with Senate amendments thereto, concur in the Senate amendments.

The Clerk read the title of the bill.

The Clerk read the Senate amend- nts, as follows:

Page 1, line 10, strike out all after "Bonds" to and including "purchaser", in line page 2.

Page 2, after line 9, insert:

SEC. 2. (a) The lands herein described not be sold after the date of enact- of this act to any purchaser, other the Blackfeet Tribe or a member there- unless (1) at least 60 days prior to such the Superintendent of the Blackfeet ncy shall have been served with notice the terms thereof and such notice, to- her with a description of the lands, and offer by the owner thereof to sell such is upon the terms specified in such notice the Blackfeet Tribe or any member there- shall have been posted for such period time in a conspicuous public place at n agency, and (2) prior to the expira- of such 60 days no bona fide offer to chase such land upon the terms specified such notice, or upon terms more favor- to the owner, shall have been made by Blackfeet Tribe or any member thereof reported to the Superintendent of the ckfeet Agency.

(b) A certificate of the Superintendent the Blackfeet Agency stating that notice the proposed sale was given and posted accordance with the provisions of clause (1) of subsection (a) and that no offer was received in accordance with clause (2) of such subsection shall, when filed and recorded in the office of the county clerk and recorder of the county in which such lands are situated, be conclusive evidence of compliance with this section.

"(c) That, if the land is purchased by the Blackfeet Tribe or a member thereof, title shall be conveyed by deed to the United States in trust for the purchaser, and if the land is purchased by a non-Indian a patent in fee shall be issued to the purchaser."

The SPEAKER. Is there objection to the request of the gentleman from Oklahoma?

Mr. MARTIN of Massachusetts. Mr. Speaker, reserving the right to object, will the gentleman explain what the Senate amendments are?

Mr. MORRIS. Mr. Speaker, I may say to the gentleman from Massachusetts that the only purpose of the amendment is to give preference right in the purchase of this land to a member of or to the tribe of Blackfeet Indians.

Mr. MARTIN of Massachusetts. They live on the reservation at the present time, do they?

Mr. MORRIS. Yes, sir.

The SPEAKER. Is there objection to the request of the gentleman from Oklahoma?

There was no objection.

The Senate amendments were concurred in.

A motion to reconsider was laid on the table.

AMENDING SECTION 503 (B) OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT

Mr. MITCHELL. Mr. Speaker, by direction of the Committee on Rules, I call up House Resolution 354 and ask for its immediate consideration.

The Clerk read as follows:

Resolved, That immediately upon the adoption of this resolution it shall be in order to move that the House resolve itself into the Committee of the Whole House on the State of the Union for the consideration of the bill (H. R. 3298) to amend section 503 (b) of the Federal Food, Drug, and Cosmetic Act. That after general debate, which shall be confined to the bill and continue not to exceed 2 hours, to be equally divided and controlled by the chairman and the ranking minority member of the Committee on Interstate and Foreign Commerce, the bill shall be read for amendment under the 5-minute rule. At the conclusion of the consideration of the bill for amendment, the Committee shall rise and report the bill to the House with such amendments as may have been adopted and the pervious question shall be considered as ordered on the bill and amendments thereto to final passage without intervening motion except one motion to recommit.

Mr. MITCHELL. Mr. Speaker, I yield myself 15 minutes.

Mr. Speaker, this resolution will bring up for consideration H. R. 3298 introduced by the gentleman from North Carolina [Mr. DURHAM]. It is fully explained in a very excellent report submitted by the gentleman from Mississippi [Mr. WILLIAMS] of the Committee on Interstate and Foreign Commerce.

The bill has two specific aims:

First. It strengthens the protection of the public health against dangerous abuses in the sale of potent drugs without prescriptions.

Second. It relieves the public and retail druggists from unnecessary restrictions on dispensing of drugs which can be used safely without medical supervision.

I think that it is a bill to protect the public health and also a bill for the relief of more than 80,000 pharmacists in the Nation's 47,000 drug stores who fill nearly 600,000,000 prescriptions every year. These professional men perform a most important service and should be assisted in that service to the extent possible through wise legislation.

Retail druggists and manufacturers agree that most of the provisions of the bill are not controversial. The present Food, Drug, and Cosmetic Act in section 503 (b) recognizes only "a written prescription signed by a physician, dentist, or veterinarian." This is unnecessarily burdensome on both the public and the druggist. The evidence is conclusive that good medical practice today requires the use of the telephone in prescribing medicines. Under appropriate safeguards a pharmacist should be allowed to fill and refill prescriptions when the physician authorizes him to do so by telephone.

The present law does not authorize pharmacists to refill any prescription without the written authorization of the doctor. This is unrealistic. House bill 3298 will permit the refilling without restriction of prescriptions for drugs that can safely be taken by a layman without medical supervision. But the bill requires that before a prescription for a habit-forming drug, a dangerous drug, a drug that is otherwise unsuitable for use by a layman, or a new drug that is limited to professional use can be refilled the doctor must be consulted and his authority obtained. Everyone concerned agrees with these provisions.

A regulation under the present law divides drugs into two classes:

First, drugs that are not suitable for use except under the supervision of a physician; and second, drugs which are suitable for use by laymen in self-medication.

The present law and the regulation has not accomplished its objective. The practical result has been that retail pharmacists have on their shelves the same drug manufactured by different firms and with different labels. When the product bears the statement: "Caution: To be dispensed only by or on the prescription of a physician," the druggist may not sell it without a prescription. The same product, however, in a package bearing directions for use may be sold without a prescription. When this situation is repeated many times in the case of different drugs it brings about confusion which affects both the public and the pharmacist. The bill is designed to end this confusion.

The means chosen to divide drugs into two classes: First, prescription drugs; second, drugs for over-the-counter sale, is controversial. The retail druggists urge that there be one authority empowered to propose a list of drugs for prescription sale only. If no one objects the list would be promulgated without

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force and effect of law. If objection is raised the Administrator would be required to announce and subsequently hold a public hearing. The druggists say that the Food and Drug Administration, under the supervision of the Federal Security Agency, is the logical governmental authority to prepare the prescription list. No alternative agency has been suggested.

The purpose of the hearing would be to receive the testimony of experts qualified by scientific training and experience. The expert testimony would deal with the question of whether or not the drug could be safely used without medical supervision including the question of whether or not the drug is one that the layman can use without medical supervision as an effective weapon against his disease. In other words, whether or not he could be told by directions how to regulate the dosage in relation to temperature or other symptoms and thus make effective use of the drug. The Administrator would be required to base his decision solely on the evidence taken at the hearing and judicial review comparable to that provided in the Administrative Procedure Act would be available to any interested person.

Testimony before the Rules Committee was to the effect that drug manufacturers opposed this delegation of power. They prefer to have the list made by individual lawsuits brought in the Federal courts. Testimony was presented that this case-by-case method of judicial determination would unnecessarily and unfairly involve retail druggists in court proceedings. These would need to be brought against retail pharmacists to determine what drugs should be restricted to prescription sale and what drugs could be sold over the counter. The druggist wants to know in advance what drugs he can properly sell without prescription. He does not want to be subjected to expensive litigation to determine how he must dispense each drug.

The real issue for the Congress to decide is whether as a matter of public policy it is best to decide before a man subjects himself to criminal prosecution whether a drug which he manufactures or sells in his drug store should be sold on prescription or can be sold over the counter.

The manufacturer argues that it would be better to accept the risk of criminal prosecution than to authorize in advance administrative determination even though that determination were controlled by statutory standard and subject to procedures comparable to those set forth in the Administrative Procedure Act. The Rules Committee felt that with a division of 19 to 4 in the House Committee on Interstate and Foreign Commerce that this issue is an appropriate one for settlement through debate on the floor and, therefore, recommends an open rule allowing 2 hours of debate.

In view of the fact that there is controversy as to this legislation, may I read into the RECORD some letters and telegrams which correctly indicate the approval of this legislation on the part of both retail druggists and the College of Pharmacy faculty in the State of Washington:

SEATTLE, WASH., *July 19, 1951.*

Representative HUGH B. MITCHELL,
New House Office Building, Washington, D. C.:

H. R. 3298 is necessary to avoid much confusion now existing in the dispensing of prescriptions. At the same time it will cut the cost of medication to the patient. This bill has been studied by the association and has its unanimous consent. Will appreciate your efforts in its passage.

R. E. DUCKERING,
Executive Secretary, Seattle-King County Retail Druggists Association.

SEATTLE, WASH., *July 19, 1951.*

Hon. HUGH B. MITCHELL,
New House Office Building, Washington, D. C.:

Pharmacists of Washington in convention in Yakima unanimously endorsed Durham-Humphrey bill. Evasion of responsibilities on the part of drug manufacturers in proper labeling, plus stupid regulations now prevailing, make for unnecessary burden and expense to both pharmacists and patients. Freedom to pharmacists to accept medical orders by telephone for nondangerous drugs would cut medical expense to the public. Your leadership in helping pilot this bill from committee and through the House would be appreciated by pharmacists and public alike throughout the State.

GRAHAM A. CONDIE.

UNIVERSITY OF WASHINGTON,
COLLEGE OF PHARMACY,
Seattle, Wash., July 18, 1951.

Congressman HUGH B. MITCHELL,
Washington, D. C.

DEAR CONGRESSMAN MITCHELL: I am writing to you with a sincere hope that you will give favorable consideration to H. R. 3298 (the Durham-Humphrey bill).

Although I am not a practicing pharmacist, I am deeply interested in promoting the best interests of pharmacy and the pharmacists. This bill definitely is a benefit to the pharmacist, the physician, and the public at large and is certainly consistent with the best practice of pharmacy. The pharmacists are striving to render the best public health service consistent with the profession, and I am sure that the passage of this bill will favor this service. Even the young people who are graduating from our colleges of pharmacy in general are looking to our representatives in Congress to assist in this important matter.

Any consideration that you will give in bringing this bill before the committee and in accomplishing its successful passage will be appreciated.

Very sincerely,

FOREST J. GOODRICH, *Dean.*

UNIVERSITY OF WASHINGTON,
COLLEGE OF PHARMACY,
Seattle, Wash., July 18, 1951.

Congressman HUGH B. MITCHELL,
Washington D. C.

DEAR CONGRESSMAN MITCHELL: I am writing to you to ask your support for H. R. 3298 (the Durham-Humphrey bill).

I feel that this bill is in the best interests of the profession of pharmacy and the public as well. Since the pharmacists are striving to render the best public-health service possible, I am sure that the passage of this bill will favor this service.

Any consideration that you may give in bringing this bill before the committee will be considered a great service by all who are interested in pharmacy.

Very truly yours,

LOUIS FISCHER,
Professor of Pharmaceutical Chemistry.

WASHINGTON STATE PHARMACEUTICAL ASSOCIATION,
Seattle, July 18, 1951.

Representative HUGH B. MITCHELL,
New House Office Building,
Washington, D. C.

DEAR CONGRESSMAN: I received word that the Durham bill, H. R. 3298, is now in the rules committee, after receiving favorable action during a public hearing in the Inter-State and Foreign Commerce Committee.

This bill is a needed amendment to the Federal Food and Drug and Cosmetic Act, and has an endorsement of the Administrator of the Food and Drug Administration.

It outlines the proper procedure that the pharmacist must follow in refilling of prescriptions and also legalizes telephoning of prescriptions from the physician, which is so necessary under the present conditions of medical care for the general public.

This bill has the unanimous endorsement of the members of our Association and I respectfully request that you use your influence to see that this bill comes out on the floor.

Respectfully yours,

H. E. HENDERSON,
Executive Secretary.

Mr. AUGUST H. ANDRESEN. Mr. Speaker, will the gentleman yield?

Mr. MITCHELL. I yield to the gentleman from Minnesota.

Mr. AUGUST H. ANDRESEN. Is it the gentleman's understanding that if the Administrator decided that some of these popular headache tablets that are advertised, and that are quite effective, could only be secured on prescription, it would be necessary for an individual to go to a doctor and get a prescription before he could buy these headache tablets?

Mr. MITCHELL. If he should decide that on the basis of the legislative standards set up in this bill and were upheld by the board of experts, I presume that would be true.

Mr. SABATH. Mr. Speaker, will the gentleman yield?

Mr. MITCHELL. I yield to the gentleman from Illinois.

Mr. SABATH. Is it not a fact that the evidence disclosed that this is in the interest of the thousands of druggists, that it would eliminate their trouble and annoyance, and at the same time benefit the public, so that they would not be obliged to get a duplicate prescription from a doctor and pay a double fee, or sometimes a triple fee, to get a prescription filled out, when the product could be sold without a new prescription from the doctor?

Mr. MITCHELL. My chairman is correct.

Mr. WILLIAMS of Mississippi. Mr. Speaker, will the gentleman yield?

Mr. MITCHELL. I yield.

Mr. WILLIAMS of Mississippi. In response to the question asked by the gentleman from Minnesota, if he will read the bill he will find in it this language, which I believe answers his question. The Administrator shall base his determination—and I quote now from the bill—"on the basis of opinions generally held among experts qualified by scientific training and experience to evaluate the safety and efficacy of such drug."

In my opinion, and apparently in the opinion of the committee, that eliminates the danger of any arbitrary ac-

use of the authority to do this by the Administrator.

Mr. AUGUST H. ANDRESEN. I regret to say to the gentleman that I do not have a great deal of confidence in the present Administrator. He may do most anything in spite of expert opinion.

Mr. MITCHELL. The gentleman understands that the Food and Drug Administration reaches the conclusions, which are just acted upon by the Administrator. There has been no complaint against the Food and Drug Administration on its administration of similar provisions regarding habit-forming drugs.

Mr. AUGUST H. ANDRESEN. I have had considerable experience with the Food and Drug Administration during the past 18 years. Some of the actions they have taken have been absolutely arbitrary and contrary to the recommendations of the experts.

Mr. BONNER. Mr. Speaker, will the gentleman yield?

Mr. MITCHELL. I yield to the gentleman from North Carolina.

Mr. BONNER. If this bill becomes law, would it affect patent medicines and household remedies that have been customarily sold by rural stores and in suburban areas back through the years? Would those drugs have to be approved by the Administration before they could be sold?

Mr. MITCHELL. In my opinion they would not be affected.

Mr. BONNER. I want that to be clear. The gentleman says in his opinion they would not.

Mr. O'HARA. Wait a minute; that is completely wrong.

Mr. SPRINGER. Mr. Speaker, will the gentleman yield?

Mr. MITCHELL. I yield to the gentleman from Illinois.

Mr. SPRINGER. It is my understanding that rural stores that have sold proprietary medicines can continue to do so under this bill. Is that the gentleman's opinion?

Mr. MITCHELL. The board of experts would have to reach a conclusion on whether these remedies fall within the defined categories.

Mr. SPRINGER. That has been formerly governed by State law, has it not?

Mr. MITCHELL. I will have to refer you to the gentleman from Mississippi [Mr. WILLIAMS], of the committee.

Mr. WILLIAMS of Mississippi. Unless the drugs should come within this category, that is the category within the definition of subsection (B) of section 201 of this bill, which defines a dangerous drug or a prescription drug as follows:

> because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, has been determined by the Administrator, on the basis of opinions generally held among experts qualified by scientific training and experience to evaluate the safety and efficacy of such drug (and, where scientific hearing is required by paragraph (B), on the basis of evidence adduced at such hearing by such experts), to be safe and efficacious for use only after professional diagnosis by, or under the supervision of, a practitioner licensed by law to administer such drug.

Unless it comes within that standard, the drug can be sold over the counter.

Mr. SPRINGER. Is it not true, then, under this bill that you are transferring these proprietary medicines which formerly have been sold, as the gentleman from North Carolina has described, by rural grocery stores to the situation where now it is going to be determined by this Administrator as to how they shall be sold? Is that not true?

Mr. WILLIAMS of Mississippi. That is stated in the law. Unless they are dangerous drugs the Administrator does not put them on his list. It will not affect the sale of Watkins products, for instance, and various other products.

Mr. O'HARA. May I make a statement in regard to a question of the gentleman from North Carolina?

Mr. BONNER. I do not think the question has ever been answered.

Mr. O'HARA. No; it has not. I will say to the gentleman, frankly, there are about 30,000 drug items, including these so-called patent medicines that under this bill are going to be turned over to Mr. Oscar Ewing, as Administrator of the Food and Drug Administration under the Federal Security Agency, and he will then be charged with making the decision of whether they must be prescription drugs, or over-the-counter items, such as patent medicines.

Mr. BONNER. I asked the gentleman from Washington whether all these different drugs and all these patent medicines have to be taken up item by item to determine whether or not they could be sold in the customary manner as they have been in the past.

Mr. HARRIS. Mr. Speaker, will the gentleman yield?

Mr. MITCHELL. I yield.

Mr. HARRIS. They do not have to be taken up by the Administrator to determine their status on an individual basis. For instance, there are several hundred types of aspirins which I am sure the gentleman includes in that category that he mentioned of drugs being sold over the counter. The Administrator would not have to take each one of those types of aspirins and make that determination. Those which, by virtue of long tradition and custom are considered to be safe over-the-counter drugs would not be affected whatsoever.

Mr. BONNER. The gentleman from Mississippi just read about alcoholic contents. I asked the gentleman and he read from the bill about alcoholic contents; did he not?

Mr. HARRIS. No; the gentleman read from the bill the standard which was set up.

Mr. BONNER. Just to name a specific drug that has become very popular, consider this drug Hadacol. Will people have to go to doctors to get a prescription for Hadacol?

Mr. HARRIS. No; Hadacol would not be affected. It would not come under this at all.

Mr. MITCHELL. Mr. Speaker, the report of the committee states:

> Under this standard a drug will be adjudged a prescription drug if because of its toxicity or any other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, it is unsafe or inefficacious for use without professional supervision.

Mr. Speaker, in reference to the statement of the gentleman from Illinois, I would like to read a telegram I received from Mr. H. E. Henderson, the executive secretary of the Washington State Pharmaceutical Association:

> SEATTLE, WASH., *July 18, 1951.*
> Representative HUGH B. MITCHELL,
> *New House Office Building,*
> *Washington, D. C.:*
>
> The druggists of this State, being entirely familiar with the provisions of H. R. 3298, urgently request that you use your efforts to secure favorable passage of this measure. We in our association have discussed it and are familiar with all of its ramifications.

This telegram was sent following a telephone conservation in which I pointed out that some were contending that pharmacists did not understand the amended bill.

The faculty of the College of Pharmacy of the University of Washington has written me to the same effect. They feel this legislation is necessary to straighten out the problems in the drug industry.

The SPEAKER. The time of the gentleman has expired.

Mr. ALLEN of Illinois. Mr. Speaker, I yield myself such time as I may require.

Mr. Speaker, this rule makes in order H. R. 3298, a bill designed to amend the Federal Food, Drug, and Cosmetic Act. It is an open rule and if adopted provides for 2 hours of general debate after which it is open to amendment under the 5-minute rule.

The primary purpose of this bill is to correct the uncertainty in the present law regarding druggists refilling prescriptions. The Food and Drug Administration has announced that under the present law a druggist may not fill an oral prescription or refill a written prescription unless specifically authorized by the prescribing physician. H. R. 3298 permits the use of oral prescriptions in the case of all drugs. However, in the case of habit-forming drugs, an oral prescription would have to be reduced promptly to writing and filled by a druggist. This is the part that retail druggists desire, and as far as I have been able to ascertain there is no objection.

All opposition to this bill centers around the extraordinary powers proposed to be granted to Federal Security Administrator Oscar Ewing. If this bill is not amended, Oscar Ewing will have the power under this bill to determine what drugs will be sold; and, if they are permitted to be sold, whether or not they will be sold over the counter or upon prescriptions. This is the same Oscar Ewing who is the original sponsor of socialized medicine, as well as a recent advocate of free medical aid for persons over 65 years of age. In my opinion, this is an unjustifiable delegation of power to an administrative agency. That is the reason I have received scores of communications from members of the medical profession back home opposing

paragraph B which grants Oscar Ewing all this power.

I am of the belief that Congress has already delegated too much authority to departments and agencies and the further delegation of power tending to the socialization of pharmacy, dentistry, nursing, and medicine merits our most serious consideration.

Since I have been in Congress I have continually opposed the granting of excessive powers to bureaucrats. A review of the legislation proposed by Oscar Ewing clearly shows that he is a confirmed adherent to the socialization of many of our institutions and professions. That is the reason the doctors in our districts are opposed to paragraph B. That is the reason various State pharmaceutical associations are opposed to paragraph B. That is the reason the national medical association is opposed to paragraph B.

All opposition to this bill would be eliminated if paragraph B is eliminated. This can be done if paragraph B is stricken and in lieu thereof the following be substituted:

(B) Because of its toxicity or other potentiality for harmful effect or the method of its use or the collateral measures necessary to its use is not safe for use except by or under the supervision of a practitioner licensed by law to administer such drug.

I understand such an amendment is to be offered by a member of the committee having jurisdiction.

Mr. JAVITS. Mr. Speaker, will the gentleman yield?

Mr. ALLEN of Illinois. Not just at this moment.

The reason there is so much controversy about this bill is that the retail druggists are for the part of the bill which permits refills. They have sent many telegrams to Members of this House. We are all agreed about that. On the other hand, the American Medical Association have sent telegrams opposing paragraph B. I have received many telegrams from my local doctors back home who are dealing directly with the druggists. I believe they are all opposed to paragraph B.

I have a telegram from the American Medical Association. They oppose paragraph B. They say:

American Medical Association wishes to advise that it filed statement at close of hearings opposing H. R. 3298 which unfortunately was not printed with hearings. Association favored original Durham bill relating to refilling prescriptions but objects very definitely to later addition which would give Federal Security Administrator power to determine therapeutic value of drugs. Such authority should remain with physicians and pharmacists if public interest is to be respected. This provision gives Federal Security Administrator unnecessary and unwarranted power to regulate the dispensing of drugs.

Then, I have one from the National Pharmaceutical Association. These people are druggists. They say:

Difference between various groups and drug industry on proposed form of H. R. 3298 will be considered at annual convention and request you to withhold action until our association of 25,000 members can give consideration to the revised bill.

Mention has been made today of proprietary medicine sold in country stores and drug stores, mentioned, I believe, by the gentleman from North Carolina, asking whether the Administrator would be given the power to determine what drugs and medicine could be sold over the counter in drug stores if section (b) of this bill is adopted.

Mr. BONNER. Mr. Speaker, will the gentleman yield?

Mr. ALLEN of Illinois. I yield.

Mr. BONNER. I am not talking about country drug stores. I am talking about country stores that have been selling patent medicines, household remedies, for years. I want to know whether one man is going to be given the power to decide whether or not such medicine and remedies can be sold only by a doctor's prescription, whether a man has got to go to a doctor to get a dose of Bromo-Seltzer.

Mr. ALLEN of Illinois. I may say to the gentleman from North Carolina that that is my understanding. Under this bill as presently written Mr. Ewing would determine which ones would come under prescription. It is an exaggeration, but he could go so far as to require a prescription for milk of magnesia or for aspirin.

Mr. JAVITS. Mr. Speaker, will the gentleman yield?

Mr. ALLEN of Illinois. I yield.

Mr. JAVITS. I wish to call the gentleman's attention to the strange wording of paragraph (b). It does not say "which has been determined by the Administrator to be safe and efficacious;" it says "has been determined by the Administrator on the basis of opinion generally held among experts qualified by scientific training and experience."

I say that with such attitude as that the Administrative Procedure Act would not control the Administrator at all.

Mr. MORANO. Mr. Speaker, will the gentleman yield?

Mr. ALLEN of Illinois. I yield.

Mr. MORANO. Has the gentleman any idea as to whether an amendment will be offered to delete that section from the bill, and if so, will it emasculate the bill?

Mr. ALLEN of Illinois. I understand such an amendment will be offered. If the committee does not offer it I will offer it myself, which will bring the bill into conformity with the wishes of the drug stores back home as to the provisions regarding refilling, but which will take away from this Oscar Ewing the power to issue orders and regulations affecting drugs and medicine.

Mr. MORANO. I want to vote for such an amendment but I also want to vote for a bill that will enable the druggist to refill prescriptions.

Mr. ALLEN of Illinois. I agree with the gentleman; I feel the same way about it and I think a great majority of the Members of the House feel as we do.

Mr. BENNETT of Michigan. Mr. Speaker, will the gentleman yield?

Mr. ALLEN of Illinois. I yield.

Mr. BENNETT of Michigan. On this question raised by the gentleman from North Carolina, under the provisions of the bill the authority to do the thing he fears might be done is there. How far the Administrator will exercise his authority, of course, is not known. As has been pointed out there are 30,000 drugs. This is about the mechanics of the situation: The Federal Security Administrator if he decided, let us say, to put Bromo-Seltzer on the prescription list, a thing which has been sold over the counter for years, he would have three, four, or five experts testify that in their opinion it was a dangerous drug, not safe or efficacious to be sold over the counter at drug stores. The drug industry would present experts who would testify to the contrary. Then there would be a conflict of medical opinion and the final authority under [illegible] decision as to whether or not the sale of the drug should be by prescription or over the counter would lie with the Administrator. He would have final arbitrary authority. That is one of the principal objections to that section.

Mr. ALLEN of Illinois. I thank the gentleman for his usual sound logic and reasoning.

Mr. O'HARA. Mr. Speaker, will the gentleman yield?

Mr. ALLEN of Illinois. I yield.

Mr. O'HARA. My distinguished colleague from New Jersey [Mr. WOLVERTON] inquired of the Administrator, Mr. Ewing, when he testified in connection with this bill as to aspirin, and this is what Mr. Ewing said:

Well, as of today, I would say "No"—

Whether it would have to be on the list—

but I think you have to recognize that under this bill you might have an Administrator who would call a hearing to put aspirin on the list of dangerous drugs. If he held that aspirin was a dangerous drug and that was appealed to the circuit court of appeals and they upheld it, then you would be in that situation.

Mr. Ewing frankly says that is the situation under this bill. Let me say that you have in that connection on appeal the language of the Food and Drug Act which says in effect that if the opinion, the judgment, of the Administrator is supported by substantial evidence, which means practically any evidence, the Circuit Court of Appeals has to affirm that decision. So what we have is a tremendous power given to one man to make a decision that is all important to the people in your community and mine.

Mr. HARRIS. Mr. Speaker, will the gentleman yield?

Mr. ALLEN of Illinois. I yield to the gentleman from Arkansas.

Mr. HARRIS. I should say, in response to the statement read by my distinguished colleague, a member of the committee, the gentleman from Minnesota [Mr. O'HARA] that the statement of the Administrator referred to the original Durham bill which did give the Administrator unlimited authority to go as far as he wanted to; but since then the committee wrote into the bill the standards that are set up here, which would, of course, limit the administrative authority to make such a far-reaching determination.

Mr. WILLIAMS of Mississippi. Mr. peaker, will the gentleman yield?

Mr. ALLEN of Illinois. I yield to the entleman from Mississippi.

Mr. WILLIAMS of Mississippi. Of ourse, I agree with my distinguished iend from Arkansas, but in response to hat the gentleman from Michigan said few minutes ago about putting aspirin this list, I may say that the commit- e heard and went over all of these rguments. Amendments were offered, nendments were voted on, and the mmittee voted by a vote of 19 to 4 to clude the language that is contained in is bill, with the administrative list and ith an administrative and judicial re- ew. If the Administrator should act bitrarily, and place such an innocuous ug as aspirin on this list, and I am ing to read from the bill:

Any interested person may file with the dministrator a petition proposing the mak- g of a determination, or the modification a determination made or proposed to be ade, by the Administrator pursuant to sub- ragraph (B) of paragraph (1). The filing a petition for the purpose of opposing a oposed determination that a drug is one which such paragraph (B) applies shall y the operation of paragraph (1) with re- ct to such drug until a petition for judi- l review can be filed and interim relief ght under section 10 (d) of the Admin- rative Procedure Act.

Mrs. ROGERS of Massachusetts. Mr. eaker, will the gentleman yield?

Mr. ALLEN of Illinois. I yield to the ntlewoman from Massachusetts.

Mrs. ROGERS of Massachusetts. Will decision of the Administrator super- le State laws in regard to the refilling prescriptions? It would certainly be y dangerous if a prescription for the rivatives of phenobarbital could be re- ed in the States that have laws pre- ting the refilling of a doctor's pre- iption without the physician's order. re in Washington there have been number of suicides that have taken ce as a result of overdoses of bar- urates. People get a dual personal- and also as a result of that medicine ir hearts become very much weak- d. I think the Senate will pass a panion bill to one I have introduced now pending before the Ways and ans Committee which will rectify and trol that situation.

Mr. WILLIAMS of Mississippi. The ntlewoman from Massachusetts can y her fears with regard to State laws flicting with the Federal laws in this ject. If the State laws prohibit the lling of phenobarbital prescriptions, t will be prevented.

Mrs. ROGERS of Massachusetts. We uld have a national law, because the tes are not enacting these laws. I w the gentleman remembers some s of suicide as the result of an over- of phenobarbital.

Mr. ALLEN of Illinois. In conclusion, Speaker, I will say that I have hun- res and scores of telegrams objecting paragraph (b) which gives Mr. Ewing qual power.

ere is one from the New York State rmaceutical Association. They say have a membership of 6,328 repre- senting 94 percent of the druggists in New York, and they come out and oppose any part except the refilling of drugs. I mentioned the refilling of prescriptions. I mentioned that to my colleagues here because I want you to know that the druggists are for the refilling part but most of them are definitely opposed to giving Oscar Ewing the power to determine what drugs shall be sold, where, and under what conditions.

Mr. MORANO. Mr. Speaker, will the gentleman yield?

Mr. ALLEN of Illinois. I yield to the gentleman from Connecticut.

Mr. MORANO. And the capricious use of any such power would create a chaotic condition in the retail druggist business, would it not?

Mr. ALLEN of Illinois. Definitely, yes. As I have said, I think there is going to be an amendment offered by the gentleman from Minnesota which will take out paragraph (b), and in lieu thereof insert the following language, which I have previously stated:

(b) because of its toxicity or other potentiality for harmful effects or the method of its use or the collateral measures necessary to its use is not safe for use except by or under the supervision of a practitioner licensed by law to administer such drugs.

Now, this amendment, I understand, has been devised to give the doctor or the druggist the type of a bill that, so far as I can ascertain, will be satisfactory.

Mr. BENNETT of Michigan. Mr. Speaker, will the gentleman yield?

Mr. ALLEN of Illinois. I yield to the gentleman from Michigan.

Mr. BENNETT of Michigan. To illustrate the confused situation that exists with respect to this provision giving the Administrator this wide authority, there is this to say: The American Medical Association is opposed to it. The American Pharmaceutical Association, which is composed of the pharmacists who work in drugstores, and the American Drug Manufacturers who manufacture drugs, are opposed to it. The American Association of Druggists is for it, though many of its members are opposed to it.

Mr. ALLEN of Illinois. It is my understanding that the rank and file of druggists are satisfied with the refill section.

Mr. BENNETT of Michigan. But here are the people who deal with this problem from day to day intimately, the doctor, the druggist, the pharmacist, and the manufacturer. They cannot agree; in fact, most of them agree that delegation of this authority would be most unwise, and they are fearful as to how it would be exercised. I think that certainly is an unfortunate atmosphere for a bill to be presented to this House when the very people it affects cannot agree among themselves as to just what it will do.

Mr. BECKWORTH. Mr. Speaker, will the gentleman yield?

Mr. ALLEN of Illinois. I yield to the gentleman from Texas.

Mr. BECKWORTH. Is the gentleman positive that the American Medical Association as an association has definitely stated that it is opposed to this bill rather than the legislative committee of the American Medical Association?

Mr. BENNETT. Well, all of these associations are speaking through their representatives.

Mr. BECKWORTH. But has the association gone on record saying it opposes this bill as an association, or was it the committee?

Mr. BENNETT. Their legislative representatives said they were opposed to it. The Retail Druggist did not come before our committee. He was represented by a spokesman here in Washington.

Mr. BECKWORTH. It has been the impression of a good many of us that the American Medical Association actually has not taken a very definite and specific position on it, and to evidence that fact the committee wanted the doctors to come before the committee, urged and requested them to, but they never did do it at all. That is the strange thing.

Mr. ALLEN of Illinois. I do not expect to ask for a roll call upon the rule because I firmly believe that after debate this body will eliminate paragraph B, thus having a bill that will be satisfactory to the druggists, to the doctors, to the pharmacists, to the manufacturers, to the wholesalers, to the law enforcement officials, and above all to the general public.

Mr. Speaker, I reserve the balance of my time.

Mr. MITCHELL. Mr. Speaker, I yield 5 minutes to the gentleman from Illinois [Mr. SABATH].

Mr. SABATH. Mr. Speaker, when the proponents of this legislation appeared before the Committee on Rules that committee desired to know how the committee stood in reporting the bill. We were informed then that only 4 of the 25 members were opposed to it and that after many weeks of consideration and investigation and hearings 19 of the members agreed to report this legislation.

My colleague from Illinois [Mr. ALLEN] implies that Mr. Ewing, Administrator of the Social Security Agency will administer the act. He is at the head of this agency, but will not actually enforce this law or provide the rules and regulations. The administration of the act will be under the supervision of the Food and Drug Administration which has functioned for many, many years in enforcing food and drug laws.

Mr. O'HARA. Mr. Speaker, will the gentleman yield?

Mr. SABATH. The gentleman knows I am right on this. Please do not take up time on that point.

Mr. O'HARA. The gentleman is in error on that point. Under the law, let me say to the gentleman——

Mr. SABATH. Oh, yes; he will be the nominal head of it.

Mr. O'HARA. He is the Administrator under the bill.

Mr. SABATH. I know that, but he will not provide the rules and regulations that are necessary and that will

be submitted to him by the Food and Drug Administration for signature, personnel who are very familiar with this type of legislation and who have been protecting the lives of American citizens for many years.

Mr. EVINS. Mr. Speaker, will the gentleman yield?

Mr. SABATH. I yield to the gentleman from Tennessee.

Mr. EVINS. I am endeavoring to find out some information as to why the need and necessity for this particular section, because the Food and Drug Administrator has authority at the present time to confiscate and take off the market deleterious or dangerous drugs, under existing law. Also the Federal Trade Commission has authority to stop the advertising, sale, labeling, and branding of drugs that are dangerous. So why the necessity for this additional legislation?

Mr. WILLIAMS of Mississippi. Mr. Speaker, will the gentleman yield?

Mr. SABATH. I yield.

Mr. WILLIAMS of Mississippi. There is a definite need for this legislation. I am sure it will be admitted by the gentlemen on the other side who oppose this particular provision, for the reason that there is and has been for some time increasing confusion under the present provisions of the Federal Food, Drug, and Cosmetic Act as to which drugs can be legally and lawfully and properly sold over the counter and which drugs should be restricted solely to the prescription of a physician.

Mr. EVINS. I think that is a point on which some decision should be made.

Mr. WILLIAMS of Mississippi. This is for the purpose of making that determination.

Mr. SABATH. I recollect that many years ago Dr. Wiley advocated food and drug legislation to protect the American public. Gentlemen then opposed the regulations he advocated. I am surprised that some of you gentlemen are not informed or are being led astray by the manufacturers. This is legislation proposed to protect the American people. The druggists surely should be and are entitled to some protection and a better Government-regulated method in dispensing drugs to the public. There are not any finer type of businessmen serving the needs of the people of our country than the druggists and we should heed their request for this legislation. Of course, there are some doctors that may object to this legislation because it will not be necessary for a patient to go to the doctor every time a prescription has to be refilled, because many of those prescriptions can be refilled without any danger to the patients.

But of course some of the doctors will be deprived of an additional $5 or $3 or an additional $10 in the larger cities. We ought to take into consideration that when an important committee, like the Committee on Interstate and Foreign Commerce, devotes weeks and months to the consideration of legislation, it in turn is entitled to consideration. I feel this legislation is in the right direction and in the interest of the public. I have received several hundred telegrams from druggists from every section of the United States which have come to me as chairman of the Committee on Rules urging and pleading to be relieved of the uncertainty that exists today.

Mr. Speaker, I do not wish to encumber the RECORD by inserting many of the telegrams I have received, but I shall take the liberty of inserting a telegram that I received from my home city, Chicago, Ill., signed by Mr. John M. Meyers, executive secretary of the Chicago Retail Druggists' Association, and a telegram signed by Thomas J. Vratny, secretary of the Illinois Pharmaceutical Association, as follows:

CHICAGO, ILL., *July 18, 1951.*

Hon. ADOLPH J. SABATH,
House Office Building,
Washington, D. C.:

The members of the Chicago Retail Druggists Association which represents the retail drug stores owners of metropolitan Chicago, embracing the counties of Cook, Lake, Kane, Du Page, and Will, at a regularly assembled quarterly meeting held July 17, 1951, directed the undersigned to advise you of their immediate concern and interest in the favorable passage of H. R. 3298, the so-called Durham-Humphrey bill now pending before the Rules Committee. This measure seeks to amend the present Federal Food, Drug and Cosmetic Act so as to enable the retail druggists of the country to serve to public with medicaments more efficiently and more economically. In the interest of the public health the undersigned respectfully requests that you make possible the immediate consideration of this measure by the entire House membership.

JOHN M. MYERS,
Executive Secretary, Chicago Retail Druggists' Association.

CHICAGO, ILL., *July 23, 1951.*

Congressman ADOLPH J. SABATH,
House of Representatives,
Washington, D. C.:

The pharmacists of the State of Illinois especially the Seventh Congressional District beg of you to give consideration to granting a ruling for H. R. 3298 that it may get to the floor of the House for action.

THOMAS J. VRATNY,
Secretary, Illinois Pharmaceutical Association.

Consequently I feel, and even though the gentlemen on the other side, and some on this side, agree that the rule should be granted, that any Member should have the right to offer amendments to the bill as provided in the rule.

This is an open rule. If any gentleman feels that he in his wisdom can improve the bill and safeguard the interest of the people, all well and good. Let us take that up in committee when the bill is being read under the 5-minute rule.

The SPEAKER. The time of the gentleman from Illinois has expired.

Mr. ALLEN of Illinois. Mr. Speaker, I yield 2 minutes to the gentleman from California [Mr. HINSHAW].

Mr. HINSHAW. Mr. Speaker, while I have the honor of membership on this great Committee on Interstate and Foreign Commerce, I also have membership on another committee of the House, the Joint Committee on Atomic Energy. Unfortunately for me, there was a conflict in the schedules of work of those two committees at the time this bill was under consideration. I was able to attend very few of the hearings and only a part of the consideration in executive session. But I attended enough of them to know that this is one of the most complicated pieces of legislation that has ever been presented to a committee of this House and ultimately to the House itself.

It is not as simple as it might appear on the surface, or as some people who have spoken would make it appear. It is exceedingly complicated, and its importance can also be judged by the amount of interest that has been displayed in it by the various professional and trade associations throughout the country.

Just to take the opposite viewpoint from some of my colleagues on the left at the moment, I point out that while it is possible such things as aspirin and Hadacol may come within the terms of this bill, there are some very important drugs which indeed should come under it. I might point out the antibiotics, such as aureomycin, streptomycin, and triptomycin, and all of such things. Somebody should be able to determine and have authority to determine whether or not those drugs are deleterious if sold under a freely refillable prescription and whether or not prescriptions should be refilled only on doctors' orders. I am not too concerned about those harmless drugs that we have known for a long, long time; but I am concerned about some of these new and border-line cases.

This has been a subject that has been very difficult to consider in the committee. The vote to report the bill to the floor was 19 to 4. The committee itself, even among the 19 and among the 4, are not so certain that they are right. This is not an easy subject, and I beg of you in the course of this discussion for as many as possible to remain on the floor and hear the truth spoken as our various committee members see it. Let us get away from the baloney and let us stick to the truth. This is too important for us to mess around with a lot of fancy statements that do not have real substance. This is important to the health and welfare of the people of the United States as a bill relating to the administration of the Food and Drug Act.

The SPEAKER. The time of the gentleman has expired.

Mr. MITCHELL. Mr. Speaker, I move the previous question.

The SPEAKER. The question is on the resolution.

The resolution was agreed to.

Mr. CROSSER. Mr. Speaker, I move that the House resolve itself into the Committee of the Whole House on the State of the Union for the consideration of the bill (H. R. 3298) to amend section 503 (B) of the Federal Food, Drug, and Cosmetic Act.

The motion was agreed to.

Accordingly the House resolved itself into the Committee of the Whole House on the State of the Union for the consideration of the bill H. R. 3298, with Mr. COLMER in the chair.

The Clerk read the title of the bill.

By unanimous consent, the first reading of the bill was dispensed with.

The CHAIRMAN. Under the rule, general debate will continue not to exceed 2 hours, the time to be equally di-

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vided between the chairman of the committee, the gentleman from Ohio [Mr. CROSSER] and the ranking minority member of the committee, the gentleman from New Jersey [Mr. WOLVERTON].

The gentleman from Ohio [Mr. CROSSER] is recognized.

Mr. CROSSER. Mr. Chairman, I yield 10 minutes to the gentleman from Texas [Mr. BECKWORTH].

Mr. BECKWORTH. Mr. Chairman, I do not pretend to be an expert on some of the details of this legislation, but I do feel that I understand what the committee has sought to do.

The gentleman from Mississippi [Mr. WILLIAMS], who is the son of a druggist and who has had considerable drug experience, I understand, reported the bill and has undertaken to study it in detail and should be in a position to shed more light on the subject than probably any other member of the committee. I do know Representative WILLIAMS has studied the details of this legislation very carefully.

In the first place, I want it understood that Mr. Oscar Ewing did not compel the committee to do what it did. I know he did not compel me to take the position I have taken. I know he did not compel the author of the bill [Mr. DURHAM] to take the position he has taken. I know he did not compel the gentleman from Mississippi [Mr. WILLIAMS], who is the son of a druggist and knows about these matters in detail, to take the position he has taken. I know he has not compelled our colleague from Arkansas [Mr. HARRIS] to take the position he has taken. I know that is true of the gentleman from North Carolina [Mr. CARLYLE], the State from which Mr. DURHAM comes. The same fact is true, I feel, concerning the supporters of this bill.

I repeat, whether you like Mr. Ewing or whether you do not like him, he did not compel 19 members of this committee to vote for the provisions of this bill as it comes before the Committee of the Whole today.

The real reason why this committee is interested in doing something about this particular problem is because the overwhelming preponderance of evidence we had over several days of hearings illustrated the fact that there is great confusion on the part of druggists and pharmacists who are selling drugs. They are in a dilemma.

I will give some specific situations, our report contains some of them. I might say that in the past 3 weeks I have written many druggists in Texas and have received many replies. The letters I have received give practically unanimous approval of the provisions of the Durham bill. Almost without exception the letters have read like this:

"We have not known whether or not we were violating the laws as we have dispensed certain drugs.

There is a very good reason for that, because individual manufacturers themselves have been, in effect, calling the turn. It is no reflection on the various manufacturers that they would have varying opinions about certain drugs. This is what troubles the druggist. Please note the report.

On page 5 we have this statement, for example:

A sample of precipitated chalk manufactured by one manufacturer was labeled with this legend—

That is what was on the package for the druggist to go by—

"Caution: To be dispensed only by or on prescription of a physician, dentist, or veterinarian, or otherwise used only for manufacturing purposes. This restriction applies only to medicinal uses."

Another sample of the same drug manufactured by a different manufacturer carried the following directions for use:

Average dose, one-quarter teaspoon in water. May also be used as a tooth powder.

Mr. O'HARA. Mr. Chairman, will the gentleman yield at that point?

Mr. BECKWORTH. Not at this point.

What the druggist is confused by is the same product put out by different manufacturers with different instructions as to its use. Why would not that kind of thing confuse anybody who wants to do the right thing? The druggists have indicated over, and over, and over again that that is the kind of thing they are seeking to clear up and for that reason are anxious for this legislation.

Mr. O'HARA. Mr. Chairman, will the gentleman yield?

Mr. BECKWORTH. I yield.

Mr. O'HARA. The gentleman has talked about precipitated chalk. The gentleman knows it is a perfectly harmless compound that is sold at drug stores; does he not? It does not have any evil effects at all.

Mr. BECKWORTH. I do not pretend to be much of an expert even on precipitated chalk. The thing I am trying to point out is that the same commodity sold to druggists by different firms bears different legends.

Mr. O'HARA. On that point will the gentleman recognize the testimony that was in the record that some drug manufacturers sell to the druggists for over-the-counter sale; some of them sell to druggists for resale by prescription; they do not want to manufacture or sell except to druggists and physicians. Is not that true?

Mr. BECKWORTH. I think I get the gentleman's point. One of the things this bill proposes to do is to distinguish between over-the-counter drugs and prescription drugs, to make it very, very plain which is which; and why is not that a good thing? Why would not any person who is endeavoring to operate a drugstore on a legitimate basis desire to have definite information as to which is which? After all, a drug for sale over the counter is a drug that presumably is to be used for self-medication, and if one is to use it, the druggist should have the assurance that as he sells that drug over the counter he is not going to do injury to the person who buys it or be prosecuted for the sale. On the other hand, if a drug is of such a serious composition that it must be prescribed, the druggist should have definite information that it should be prescribed in order that he may know he is not making a mistake in connection with that kind of drug. What I have just said, of course, applies in the main to drugs all of the characteristics of which druggists cannot be familiar with. They may be new drugs.

Mr. BENNETT of Michigan. Mr. Chairman, will the gentleman yield?

Mr. BECKWORTH. I yield.

Mr. BENNETT of Michigan. The Federal Security Administrator has authority under present law to proceed against one or the other of the manufacturers in the case the gentleman just referred to, proceed for mislabeling; in other words, if the same drug has different labels one package is mislabeled and the Administrator has ample authority today to proceed. But he does not proceed in the cases the gentleman mentioned because there is no harm being done.

Mr. BECKWORTH. That is right, and I think that is a good example of the fairness that has characterized the Federal Administrator covering the Durham bill. If he were proceeding there would be many, many proceedings at this time; and there are examples of such confusion that were presented to our committee where serious and earnest pleas were made that we help straighten out such confusion.

The gentleman is correct, the Administrator could proceed, but it is because of the multitude of proceedings that would have to be instituted almost right now that we are undertaking to help straighten out this problem.

Mr. BENNETT of Michigan. He does not proceed in this case because no harm is being done. After all, in the case of a harmless drug, if the drug manufacturer does put a prescription label on it, who is harmed?

Mr. BECKWORTH. The record evidences cases where druggists were innocently going ahead and selling what they thought was not illegal, and yet would have to undergo proceedings because of certain decisions or opinions that they were not aware of at the time or perhaps had not been made at the time of their sale or sales. That is exactly true, and it is that kind of thing we are trying to straighten out; it is what the druggists want straightened out.

Mr. BENNETT of Michigan. In straightening it out, the fear that many people have is that the cure might be worse than the disease.

Mr. BECKWORTH. That theory is entertained by some, but I do not subscribe to it after listening to all of the testimony.

The CHAIRMAN. The time of the gentleman from Texas has expired.

Mr. CROSSER. Mr. Chairman, I yield the gentleman five additional minutes.

Mr. BECKWORTH. Mr. Chairman, the bill, other than the section that has been discussed so much under which Mr. Ewing would have the power to place certain drugs in certain categories if the facts warrant, does some other things as those of you who are familiar with it or who have studied it already are aware. It would permit the drugs to be prescribed over the telephone. Today that is not regarded as legal. Then it would permit certain refilling of prescriptions

if those prescriptions do not fall in the three prohibited categories, refilling without another prescription. As the situation exists today, a prescription presumably cannot be refilled unless on the prescription the doctor says that it can be refilled.

Mr. ROBERTS. Mr. Chairman, will the gentleman yield?

Mr. BECKWORTH. I yield to the gentleman from Alabama.

Mr. ROBERTS. I think the gentleman is making a very fine statement. I would like to go back to a question that was asked by the gentleman from Michigan. Is it not true that, under the present situation, the first the druggist knows that he is in violation of the law is when he is greeted with a warrant from some Federal officer or subjected to libel proceedings and seizure of his business and the destruction of his business? Is that not true under the present system, which is what we are trying to prevent by this legislation?

Mr. BECKWORTH. That is precisely the case.

There has been a good deal of talk about who is for this bill and who is against the bill. I think it is accurate to say that the drug manufacturers in general, that is, those who are manufacturing drugs, are opposed to the bill.

With reference to the other two categories there is considerable difference of opinion as to just what the situation is. I think it is fair to say that about 34,000 druggists who belong to the Druggists' Association or the association that has in it people who own drugstores and who are pharmacists, do favor this bill. Perhaps the other organization having some 14,000 pharmacists may be opposed to the bill. Certainly some of them are. But the thing that impressed this subcommittee was the fact that the great body of druggists, those who are in the position primarily of selling drugs, and I would say a heavy percentage of all drugs, to the American people simply want to know where they stand with reference to various drugs.

Mr. EVINS. Mr. Chairman, will the gentleman yield?

Mr. BECKWORTH. I yield to the gentleman from Tennessee.

Mr. EVINS. As a result of this legislation will there be a tightening up or a relaxation of the possibility of buying drugs by the consumer?

Mr. BECKWORTH. May I say this, in my opinion the Pure Food and Drug people of this country, who want to do a fair and reasonable job for the American people, incidentally, are for this bill. You know, a lot is said about the Federal Security Administrator, but the Pure Food and Drug people are for this legislation too. If they are against any part of it, I do not know what it is, and we have some mighty able and conscientious people down there.

In answer to the gentleman, may I say that the one item needed is certainty—certainty as to the category in which a drug should be placed, will be the product of this legislation, not necessarily a tightening up, not necessarily a loosening, but a certainty with reference to various drugs. The Pure Food and Drug people will do what they have sought to do in the past, and that is to place drugs in the category that they should be, and in such a manner that the American consuming public of drugs will be protected. That is their objective, in my opinion.

Mr. EVINS. In other words, it is the gentleman's view that there are many items in which the consumer has to get a prescription at the present time before he can acquire it, whereas later it may not be necessary to have that prescription.

Mr. BECKWORTH. In reference to an innocuous drug, the Pure Food and Drug people, through Mr. Oscar Ewing, because he happens to be the head of the agency under which the Pure Food and Drug agency operates, probably will be placed in a category where a druggist can sell it over the counter and sell it safely without fear of prosecution.

Mr. BEAMER. Mr. Chairman, will the gentleman yield?

Mr. BECKWORTH. I yield to the gentleman from Indiana.

Mr. BEAMER. Mr. Chairman, my very good friend and colleague has raised one important point. I am wondering whether or not the druggist in his district, in his State, and throughout the Nation, really know the contents of the bill. In the time that will be allotted to me I want to illustrate to the committee and to the Members of this House a situation that actually exists. In fact, they have not even read the bill. Someone from their association asked them to write us, to wire us, to contact us to support this bill. Now then, I sent out copies of the bill and I sent copies of the minority report to them and asked them to please study it, and in all of those cases they wrote to me, "Do not give any more authority to the Administrator not only on refills, but let us fight one part and support the other part."

Mr. BECKWORTH. In the first place, that question could be asked with reference to any bill which the House of Representatives considers. There always is a question as to how much the citizens of this country know about the details of given bills which we consider here. I had the same experience as the gentleman. I try to be as cautions and careful as the gentleman, so I sent out many of these bills to druggists in Texas, and I just want to say to the gentleman that the responses which I received do not correspond to the responses of the people to whom he refers. I am not doubting the gentleman, but I am just saying that the response I received from druggists in our section, in the Southwest, in Texas primarily, just do not correspond with what the gentleman says he received. Very frequently the people of different sections of our country see legislation differently, but I am convinced by and large that the druggists throughout this country know in the main what this bill is, and they are for it.

Mr. HOLIFIELD. Mr. Chairman, will the gentleman yield?

Mr. BECKWORTH. I yield to the gentleman from California.

Mr. HOLIFIELD. I want to say that I have listened very carefully to the gentleman's exposition of this bill, and I also read the report and some of the hearings very carefully. I want to compliment the gentleman on his statement before the committee this afternoon. I want to say this, if there is one field outside of the field of food regulation, where the American public has been milked out of millions and millions of dollars, it is by the patent-medicine manufacturers of the United States.

It is about time, it seems to me, that we take recognition of this fact and give some sort of protection to the people of the United States and also some sort of protection to those who are customarily called upon to sell these drugs. Looking over this bill, I think there is a great deal of merit to it. I appreciate the exposition the gentleman has given of its contents.

Mr. BECKWORTH. We did not have a lot of testimony with reference to such products as patent medicines and those remedies sold by companies like the Watkins Co. and the Rawleigh Co., companies whose personnel in my area I appreciate, but in my opinion they would be affected in no way except as they come within the scope of these three categories; habit-forming drugs, dangerous drugs, and new drugs.

Mr. HOLIFIELD. Certainly the public should be given some protection from those types.

Mr. BECKWORTH. If they meet the standards that are set up to protect the public, I think that kind of people need have no fear.

Mr. HARRIS. Mr. Chairman, will the gentleman yield?

Mr. BECKWORTH. I yield to the gentleman from Arkansas.

Mr. HARRIS. Is it not a fact that this legislation is designed and has for its purpose only one thing, that is, to protect sick people and provide for them the type and kind of product that they should have for their health and safety?

Mr. BECKWORTH. There is no question about that. That was the only thing that motivated the 19 members of the committee for this bill.

Mr. BENNETT of Michigan. Mr. Chairman, will the gentleman yield?

The CHAIRMAN. The time of the gentleman from Texas has expired.

Mr. WOLVERTON. Mr. Chairman, I yield 2 minutes to the gentleman from Texas, so that he may yield to the gentleman from Michigan.

Mr. BECKWORTH. I yield to the gentleman from Michigan.

Mr. BENNETT of Michigan. A little while ago in the debate the gentleman from Texas asked me a question as to whether the action of the legislative committee of the American Medical Association in opposing this bill was approved by the association itself. I am glad to advise him that I have been informed by Mr. Wilson of the legislative committee that the board of trustees of the American Medical Association approved the action taken by the legislative committee.

Mr. BECKWORTH. On what date?

Mr. BENNETT of Michigan. He does not say on what date.

Mr. BECKWORTH. My colleague knows I have the greatest respect for him, but the American Medical Association should know that to be most effective it should make its position known to the committee before the committee acts and, if possible, come before the committee and state its position, because our committee is one that will give consideration to the opinion and position of the American Medical Association just as it will to that of anybody else's group. Since the gentleman has brought up the position of the American Medical Association——

Mr. BENNETT of Michigan. The gentleman from Texas asked me the question as to whether the board of trustees of the American Medical Association had approved the action. I gave him the answer.

Mr. BECKWORTH. I am truly interested in getting information. May I ask the gentleman to place in the RECORD at this point the position of the American Medical Association as they stated it and the date they passed on it? I think it would be of interest to have it in the RECORD, because so far we do not have it.

Mr. BENNETT of Michigan. I will refer to it in my remarks.

Mr. CROSSER. Mr. Chairman, I move that the Committee do now rise.

The motion was agreed to.

Accordingly the Committee rose; and the Speaker having resumed the chair, Mr. COLMER, Chairman of the Committee of the Whole House on the State of the Union, reported that that Committee, having had under consideration the bill H. R. 3293) to amend section 503 (b) of the Federal Food, Drug, and Cosmetic Act, had come to no resolution thereon.

CONTROL OF EXFORTS

Mr. COLMER, from the Committee on Rules, reported the following privileged resolution (H. Res. 363, Rept. No. 777), which was referred to the House Calendar and ordered to be printed:

Resolved, That immediately upon the adoption of this resolution it shall be in order to move that the House resolve itself into the Committee of the Whole House on the State of the Union for the consideration of the bill (H. R. 4550) to provide for the control by the United States and cooperating foreign nations of exports to any nation or combination of nations threatening the security of the United States, including the Union of Soviet Socialist Republics and all countries under its domination, and for other purposes. That, after general debate which shall be confined to the bill and continue not to exceed 1 hour, to be equally divided and controlled by the chairman and ranking minority member of the Committee on Foreign Affairs, the bill shall be read for amendment under the 5-minute rule. At the conclusion of the consideration of the bill for amendment, the Committee shall rise and report the bill to the House with such amendments as may have been adopted and the previous question shall be considered as ordered on the bill and amendments thereto to final passage without intervening motion except one motion to recommit.

COMMISSION TO STUDY ANTITRUST LAWS

Mr. JAVITS. Mr. Speaker, I ask unanimous consent to address the House for 1 minute.

The SPEAKER. Is there objection to the request of the gentleman from New York?

There was no objection.

Mr. JAVITS. Mr. Speaker, I am today introducing a bill to establish a Federal Commission similar to the Hoover Commission on the revision of the antitrust laws. This bill is being introduced in the other body by the junior Senator from Oregon, Mr. MORSE.

Fundamental changes have taken place in our own economy and in the economy of the world since the antitrust laws were enacted in 1890, making a specific review vital today. The problem of gearing our vast industrial machine to the demands of world leadership both in defense and civilian production require new rules. In addition, the relationship of the United States to foreign economic systems needs redefinition in terms of what will contribute most effectively to the defense of the free world and to its maximum integrated production effort.

There has been much complaint in recent years that antitrust policies have crippled small business, particularly in its trade-association activities and in its efforts to pool resources to achieve a better competitive position, denied consumers the benefits of integration, hampered the cooperation of business in the defense effort, and sought to change drastically the geographical pattern of commerce. On the other hand, it has been charged that big business, due to policies in the last two decades, has just grown bigger, that price leadership has become price uniformity, and that the monopolistic privileges of patents are being grossly abused.

We are convinced that our system of the free economy of which the major regulatory statutes are the antitrust laws can be refreshed and revitalized through a review of the antitrust laws in the light of the problems which have been disclosed and the methods of their solution which the courts have adopted. It is time to bring the antitrust laws back to the Congress and the people who alone should determine the Nation's economic destiny. Whether the varying economic interests of the country are right or wrong about what has occurred in antitrust law decision and administration, the review will be healthy and changes can be made in the light of the new stature of the United States on the world horizon.

The text of the bill follows:

A bill for the establishment of a Commission on Revision of the Antitrust Laws of the United States

DECLARATION OF POLICY

SECTION 1. Whereas there exist under the antitrust statutes of the United States conflicts in policy as to the proper standards of conduct required to be observed by American industry; and

Whereas interpretation and administration of the said laws by the several courts and administrative agencies have not succeeded in resolving said conflicts; and

Whereas such conflicts and duplication of responsibility among enforcement agencies have resulted in unnecessary expense and burden on the Federal Government and on business;

It is hereby declared to be the policy of the Congress to promote the economy of the United States, to increase the efficiency of American business and industry, to improve quality, reduce price and increase output and real wages, and to promote the free flow of goods and services to the American people by (1) strengthening the laws prohibiting monopoly and unreasonable restraints on trade and commerce; (2) clarifying standards of conduct deemed lawful under the antitrust laws; (3) adjusting the policies of the Federal Government toward business, industry, investors, agriculture, and labor to conform with the present-day needs of the American people; (4) eliminating conflicts in policy and inconsistencies in the said antitrust laws as interpreted by the courts and administrative agencies; (5) relieving industry of responsibility under said laws for conduct performed at the request of duly constituted United States Government authorities; (6) revising Federal antitrust laws, the effect of which is to impair initiative and the development of new enterprises; (7) coordinating the activities of the Government in relation to the administration and enforcement of the antitrust laws; and (8) improving the methods and procedures of administration and enforcement of such laws.

ESTABLISHMENT OF THE COMMISSION ON REVISION OF THE ANTITRUST LAWS

SEC. 2. For the purpose of carrying out the policies set forth in section 1 of this act, there is hereby established a bipartisan commission to be known as the Commission on Revision of the Antitrust Laws (in this act referred to as the "Commission").

MEMBERSHIP OF THE COMMISSION

SEC. 3. (a) Number and appointment: The Commission shall be composed of 12 members as follows:

(1) Four appointed by the President of the United States, two from the executive branch of the Government, and two from private life;

(2) Four appointed by the President pro tempore of the Senate, two from the Senate, and two from private life; and

(3) Four appointed by the Speaker of the House of Representatives—two from the House of Representatives and two from private life.

(b) Political affiliation: Of each class of two members mentioned in subsection (a), not more than one member shall be from each of the two major political parties.

(c) Vacancies: Vacancies in the Commission shall not affect its powers but shall be filled in the same manner in which the original appointment was made.

ORGANIZATION OF THE COMMISSION

SEC. 4. The Commission shall elect a Chairman and a Vice Chairman from among its members. The Chairman shall be a Member of Congress.

QUORUM

SEC. 5. Seven members of the Commission shall constitute a quorum.

COMPENSATION OF MEMBERS OF THE COMMISSION

SEC. 6. (a) Members of Congress: Members of Congress, who are members of the Commission, shall serve without compensation in addition to that received for their services as Members of Congress, but they shall be reimbursed for travel, subsistence, and other necessary expenses incurred by them in the performance of the duties vested in the Commission.

(b) Members from the executive branch: Any member of the Commission who is in the executive branch of the Government shall each receive the compensation which he would receive if he were not a member of the Commission, plus such additional compensation, if any, as is necessary to make his aggregate salary $15,000; and he shall be reimbursed for travel, subsistence, and other

The remaining increase of $109,775 above the House bill is made up of many small items, none of which, I believe, are controversial.

It will be recalled that your committee brought on this floor a bill which called for a Federal contribution of $12,000,000—the amount authorized by substantive law. It will also be recalled that, after stanch support of this amount by every member of the District of Columbia Subcommittee on both the majority and minority side, the House reduced this by $1,200,000 by a vote of 56 to 41. In view of this directive your conferees attempted to secure conference agreement to the amount of $10,800,000, but failing in this we sought the best compromise possible and agreed to a 50–50 split, in other words $11,400,000 to be divided $10,400,000 for the general fund and $1,000,000 to the water fund.

Mr. Speaker, I do not believe that there are any other items of sufficient importance for me to take additional time of the House in describing.

The SPEAKER. The question is on agreeing to the conference report.

The conference report was agreed to.

The SPEAKER. The Clerk will report the first amendment in disagreement.

Mr. BATES of Kentucky. Mr. Speaker, I ask unanimous consent that the six amendments in disagreement may be considered en bloc, Senate amendments Nos. 10, 12, 21, 25, 26, and 28.

The SPEAKER. Is there objection to the request of the gentleman from Kentucky?

There was no objection.

The Clerk read as follows:

Senate amendment No. 10: Page 9, line 20, insert "Elementary school in the vicinity of River Terrace, Northeast."

Senate amendment No. 12: Page 10, line 15, insert "Elementary school in the vicinity of River Terrace, Northeast."

Senate amendment No. 21: Page 18, line 16, insert "The unobligated balance of the appropriation of $382,909 for furnishing and equipping the combination pediatrics and crippled children's building at Gallinger Hospital, contained in the District of Columbia Appropriation Act, 1950, shall remain available until June 30, 1952."

Senate amendment No. 25: Page 35, line 16, insert "and not to exceed $162,000 of the appropriation for 'Capital outlay, Sewer Division,' contained in the District of Columbia Appropriation Act, 1948, for increasing capacity of the sewage treatment plant, including additional sludge digestion tanks and additional sedimentation tanks, and not to exceed $12,000 of the appropriation for 'Capital outlay, Sewer Division,' contained in the District of Columbia Appropriation Act, 1947, for preparation of plans and specifications for constructing chemical treatment, sludge drying, and incineration facilities at the sewage treatment plant, are continued available for expenditure until June 30, 1952."

Senate amendment No. 26: Page 37, line 23, strike out "$1,813,000" and insert "and fluoridation of water, $1,943,000."

Senate amendment No. 28: Page 46, line 17, insert "including under the Executive Office the Budget Officer in GS–16."

Mr. BATES of Kentucky. Mr. Speaker, I move that the House recede from its disagreement to the amendments of the Senate numbered 10, 12, 21, 25, 26, and 28, and concur therein.

The motion was agreed to.

By unanimous consent, a motion to reconsider the votes by which action was taken on the several motions was laid on the table.

CALL OF THE HOUSE

Mr. HOFFMAN of Michigan. Mr. Speaker, I make the point of order that a quorum is not present.

The SPEAKER. Evidently a quorum is not present.

Mr. PRIEST. Mr. Speaker, I move a call of the House.

A call of the House was ordered.

The Clerk called the roll, and the following Members failed to answer to their names:

[Roll No. 145]

Armstrong	Engle	Pickett
Bakewell	Fine	Poage
Baring	Fisher	Poulson
Barrett	Flood	Powell
Bates, Mass.	Fogarty	Price
Blatnik	Gillette	Rabaut
Bosone	Golden	Radwan
Bow	Grant	Redden
Boykin	Green	Regan
Breen	Hall, Edwin Arthur	Richards
Brehm	Hand	Rivers
Busbey	Holifield	Rogers, Colo.
Case	Irving	Roosevelt
Celler	Johnson	Saylor
Chatham	Kearney	Scott, Hardie
Chelf	Kennedy	Scott, Hugh D., Jr.
Chenoweth	Kilburn	Scudder
Cooley	Kilday	Shelley
Coudert	King	Short
Curtis, Nebr.	Lyle	Sikes
Davis, Tenn.	McDonough	Smith, Kans.
Dawson	McGregor	Taber
Dingell	Mack, Ill.	Thomas
Dollinger	Miller, Calif.	Watts
Donovan	Morgan	Whitaker
Durham	Morton	Whitten
Eberharter	Murray, Wis.	Yates
Ellsworth	Perkins	
Elston		

The SPEAKER. On this roll call 349 Members have answered to their names, a quorum.

By unanimous consent, further proceedings under the call were dispensed with.

COMMITTEE ON BANKING AND CURRENCY

Mr. SPENCE. Mr. Speaker, I ask unanimous consent that the Committee on Banking and Currency may have until midnight tonight to file reports on a resolution and a bill, Senate Joint Resolution 78 and H. R. 3176.

The SPEAKER. Is there objection to the request of the gentleman from Kentucky?

There was no objection.

AMENDING SECTION 503 (B) OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT

Mr. WILLIAMS of Mississippi. Mr. Speaker, I move that the House resolve itself into the Committee of the Whole House on the State of the Union for the further consideration of the bill (H. R. 3298) to amend section 503 (b) of the Federal Food, Drug, and Cosmetic Act.

The motion was agreed to.

Accordingly the House resolved itself into the Committee of the Whole House on the State of the Union for the further consideration of the bill H. R. 3298, with Mr. COLMER in the chair.

The Clerk read the title of the bill.

The CHAIRMAN. When the Committee rose on yesterday the gentleman from Ohio [Mr. CROSSER] had 41 minutes remaining and the gentleman from New Jersey [Mr. WOLVERTON] had 58 minutes remaining.

The gentleman from New Jersey is recognized.

Mr. WOLVERTON. Mr. Chairman, I yield myself 21 minutes.

Mr. Chairman, the bill which is before the House for consideration at this time is one that has been given careful consideration by the Committee on Interstate and Foreign Commerce. I do not know of any legislation which the committee has had before it at any time that has been given more careful consideration than the present measure.

There may be some differences of opinion with respect to some features of the bill, but I think there is no doubt that there is unanimity of agreement so far as the objectives of the bill are concerned. I realize from the short debate yesterday and the questions asked during that debate, that there are many questions in the minds of individual members with respect to the measure. I am inclined to believe that many of the questions are due in some measure at least to the receipt of telegrams from interested parties who I am fearful do not in each instance entirely understand the provisions of the bill as reported to the House. The bill reported to the House has made many changes in the bill as originally introduced. I will depart from the usual method of presenting an argument to the House.

I will present my views and my interpretations of this bill by questions and answers in which I will endeavor to give information that will answer the questions that I think are uppermost in the minds of those who are anxious to do the right thing with respect to this legislation. I think I can best do it by this form of presentation. I ask that the Members give careful attention as I now proceed to give the questions and answers to which I have referred.

QUESTIONS AND ANSWERS ON H. R. 3298

First. Question: Why is it necessary for the Congress to consider at this time the bill H. R. 3298?

Answer: Because there has been constantly increasing confusion under the present provisions of the Federal Food, Drug, and Cosmetic Act of 1938 as to which drugs may be sold only on prescription and which drugs may be sold freely over the counter.

Second. Question: What causes this confusion?

Answer: The present provisions of the Federal Food, Drug, and Cosmetic Act of 1938 and the regulations issued thereunder with respect to prescription drugs and over-the-counter drugs are so general that drug manufacturers have differed greatly in the interpretation of these provisions and regulations, and, therefore, in many cases one and the same drug is labeled differently by different manufacturers for prescription sale and for over-the-counter sale.

Third. Question: What is the purpose of H. R. 3298?

Answer: The purpose of H. R. 3298 is to protect the public in the use of potent medicines which should be sold on prescription and to bring about uniformity in the labeling of drugs as prescription drugs and over-the-counter drugs.

Fourth. Question: What is meant by a prescription drug?

Answer: A prescription drug is a drug which may be sold by the druggist only on prescription and which must be labeled with a caution legend that it may be sold only on prescription.

Fifth. Question: What is meant by an over-the-counter drug?

Answer: An over-the-counter drug is a drug which may be sold freely over the counter and which must be labeled with adequate directions for use so that it may be used for self-medication.

Sixth. Question: Is a distinction between prescription drugs and over-the-counter drugs the only problem which is dealt with in H. R. 3298?

Answer: No, it is not. Other provisions in H. R. 3298 deal with telephone prescriptions and the refilling of prescriptions.

Seventh. Question: What does the Federal Food, Drug, and Cosmetic Act of 1938 provide at present with respect to telephone prescriptions?

Answer: The Federal Food, Drug, and Cosmetic Act of 1938 does not permit telephone prescriptions.

Eighth. Question: Should telephone prescriptions be permitted even in the case of potent and dangerous drugs?

Answer: Yes; they should be permitted because the use of the telephone in prescribing medicine is a great convenience both to the doctors and the patients and in some areas of this country telephone prescriptions are absolutely essential to the public health.

Ninth. Question: What safeguards are provided in H. R. 3298 with respect to telephone prescriptions?

Answer: Telephone prescriptions for drugs that may be sold only on prescriptions must be reduced to writing promptly by the pharmacist and must be filled by him.

Tenth. Question: What does H. R. 3298 provide with respect to the refilling of prescriptions?

Answer: H. R. 3298 provides that prescriptions for drugs that may be sold on prescriptions only may not be refilled unless the prescription itself states that it is refillable. A prescription which calls for dispensing of drugs that may be sold freely over the counter may be refilled freely even in the absence of a statement by the prescribing physician that the prescription is refillable.

Eleventh. Question: Why is a distinction made with respect to the refilling of prescriptions between drugs which may be sold only on prescription and drugs which may be sold freely over the counter?

Answer: A distinction is made because in the case of drugs that may be sold freely over the counter it is usually safe for the patient to take the medicine called for in the prescription without again consulting a physician.

Twelfth. Question: Does this mean that in the case of drugs which may be sold only on prescription refilling of prescriptions is unlawful unless specifically authorized by a physician?

Answer: Yes; it does mean that in the case of drugs that may be sold only on prescription a physician will have to authorize specifically the refilling of such prescription.

Thirteenth. Question: Does this mean additional cost to the patient because he will have to get a new prescription from the physician?

Answer: Yes; it may mean that in those cases where the patient cannot safely determine by himself whether he should continue to take the drug originally prescribed by a physician.

Fourteenth. Question: What does the present law provide with respect to the refilling of prescriptions?

Answer: The present law generally prohibits the refilling of all prescriptions unless the prescribing physician authorizes specifically such refilling. The present law makes no distinction between prescriptions for drugs that may be sold only on prescription and drugs which may be sold freely over the counter.

Fifteenth. Question: Does that mean that under the present law a prescription for aspirin may not legally be refilled?

Answer: It means just that and it is the purpose of the bill to authorize the refilling of prescriptions for over-the-counter drugs like aspirin and other commonly used home remedies.

Sixteenth. Question: Has that always been the law or has that state of affairs been brought about by Dr. Dunbar's speech in 1948?

Answer: That has been the state of the law since 1938 and Dr. Dunbar's speech merely called attention to the fact that the Food and Drug Administration in not prosecuting cases involving the unauthorized refilling of prescriptions merely winked at the law.

Seventeenth. Question: Under the bill who would determine which drugs may be sold only on prescription and which drugs may be sold freely over the counter?

Answer: Under the bill the Federal Security Administrator would make that determination on the basis of a statutory standard written into the bill defining dangerous drugs and on the basis of generally prevailing expert opinions with respect to the safety of such drugs.

Eighteenth. Question: Under the present law who determines what is a prescription drug and an over-the-counter drug?

Answer: Under the present law the Food and Drug Administration brings a suit for misbranding and in the course of such suit the court determines whether a particular drug is a prescription drug or an over-the-counter drug.

Nineteenth. Question: Why is it desirable to change the law in this respect and to give the Federal Security Administrator power to determine which are prescription drugs and which are over-the-counter drugs?

Answer: There are approximately 30,000 drug items which could require 30,000 lawsuits to determine under the present law which are prescription drugs and which are over-the-counter drugs.

Twentieth. Question: How is the power of the Administrator circumscribed and how are the rights of interested parties safeguarded?

Answer: The Administrator is called upon to make his determination in accordance with a specific statutory standard defining dangerous drugs, and his determination must be based upon generally prevailing opinions of experts with respect to the safety of such drugs. If any interested party opposes a proposed classification of a drug or seeks a change in an existing classification, hearings must be held in the course of which qualified experts would be called upon to testify. The determination of the Administrator is reviewable in the circuit court of appeals.

Twenty-first. Question: Is the grant of this power unusual?

Answer: No; the grant of this power is not unusual at all. There are, under the bill, three classes of prescription drugs; first, habit-forming drugs; second, dangerous drugs; and, third, new drugs. In the case of the first and the last classes, the Administrator already has the power that the bill would give him with respect to the second class of drugs.

Twenty-second. Question: Must this power be given to the Administrator or is there another way of creating uniformity?

Answer: The committee has studied carefully all the alternatives that have been proposed and reluctantly has come to the conclusion that there is no way of bringing about uniformity without somebody making the decision as to which drugs are prescription drugs and which are over-the-counter drugs.

Twenty-third. Question: Who favors the grant of this power to the Administrator?

Answer: The National Association of Retail Druggists favor the grant of this power not because they merely want the Administrator to have additional power, but because they seek uniformity in the labeling of drugs and no other way is open by which this objective can be achieved.

Twenty-fourth. Question: What is the National Association of Retail Druggists?

Answer: It is an association of approximately 35,000 drug-store owners.

Twenty-fifth. Question: Who opposes the legislation?

Answer. Nobody opposes the legislation in its entirety. Everybody is agreed that the provisions of the bill with respect to telephone prescriptions and with respect to the refilling of prescriptions are necessary and desirable changes in the present act. Everybody further contends, publicly at least, that uniformity is desirable. However, several organizations of manufacturers and pharmacists have opposed, on principle, the grant of additional authority to the Administrator to secure uniformity.

Twenty-sixth. Question: Have alternative proposals been suggested by the opposing groups in order to secure the desired uniformity?

Answer: The answer, in effect, is no, because the proposal which has been made by the opposing organizations involves retaining the present law which possibly involves 30,000 lawsuits before uniformity can be achieved.

Twenty-seventh. Question: Could uniformity be secured without legislation purely on the basis of an understanding among manufacturers?

nswer: Theoretically, the existence his possibility cannot be denied. In al practice, however, all attempts to re such understanding have failed.
wenty-eighth. Question: What is the ncipal reason for the failure of such rmal understanding?
nswer: The principal reason for this ure is that quite a number of manuturers actually are opposed to unimity and prefer the continuance of present labeling which restricts ny safe drugs to prescription sales.
wenty-ninth. Question: Why should e manufacturers desire to restrict gs to sale on prescription only alugh they could safely be sold over counter without a prescription?
nswer: Several drug manufacturers e traditionally in their trade catered physicians and registered pharmas. Many physicians prefer to buy or mote medicines of firms who sell their gs in this way.
hirtieth. Question: Are there any sons other than the traditional trade tions of particular drug manufacers?
nswer: Yes; a possible other reason hat by labeling drugs for prescripn sale only, such drug manufacturavoid the responsibility of placing such drugs correct directions for use.
hirty-first. Question: Is the general blic benefited by the requirement that safe drugs bear directions for use?
nswer: Yes; the public is benefited this requirement because self-mediion is possible only if adequate and rect directions for use are set forth the labels of safe drugs.
hirty-second question: Are the proions of H. R. 3298 burdensome for the all druggist as is claimed by some oping the bill? More particularly, must druggists consult at all times the deral Register in order to escape reponsibility under the Food and Drug ?
nswer: H. R. 3298 greatly improves position of the druggists in that it uires the clear-cut labeling of all gs, thus, in practice, enabling the ggists who buy from reputable conns to rely on the manufacturers' els. In those exceptional cases where drug manufacturer disregards the eling requirements of the bill and ce an incorrect label on a drug, the ggist theoretically is responsibile der the law. However, he can pro- himself by checking the Administor's list and, furthermore, enforcent of the law is traditionally directed ainst the source of the evil, namely, manufacturer who falsely labeled a g.
hirty-third question: Does this bill vance socialized medicine?
Answer: It certainly does not. The ctor's right to prescribe any medicine sees fit remains completely unaffected the bill. Instead of furthering cialized medicine, the bill actually minates some of the present restrictive ovisions of the law.
hirty-fourth question: Does the bill trict the public's choice of remedies?
Answer: No. It guarantees that all ugs that can be safely used by a layman shall be labeled with complete directions which the purchaser can follow without medical advice. It does prevent the sale without prescription of drugs that would harm the purchaser if he took them without professional advice. It is distinctly advantageous to the public.

Thirty-fifth question: Does the bill authorize the Administrator to place drugs on the prescription list by relying on the opinions of experts employed in the agency?

Answer: No. The Administrator must base his action only on opinions generally held by experts qualified by scientific training and experience to evaluate the safety of drugs.

Thirty-sixth question: Does this bill establish a licensing control system over all drug manufacturers?

Answer: Certainly not. The bill has no provision whatever that directly or indirectly mentions licensing. The bill simply authorizes the Administrator to say, after public proceedings, that a particular drug must thereafter be sold on prescription. This enables the manufacturer to know before he violates the law that his drug must be sold on prescription only.

Thirty-seventh question: Does this bill make it possible for the Administrator to put such household remedies, as bromo-seltzer, milk of magnesia, and citra carbonate on prescription?

Answer: Of course not. It requires the Administrator to respect the opinions generally held that these articles are safe for self-medication.

Thirty-eighth question: What is the position of the doctors?

Answer: Representatives of the American Medical Association were present at the committee hearings but refused to testify. Some members of the association, however, have expressed their disapproval of the bill because it vests additional powers in Mr. Ewing whom they distrust. In my opinion this is distinctly unfounded in this particular instance.

Thirty-ninth question: Does this bill authorize grocery stores, supermarkets, and house-to-house vendors to sell drugs?

Answer: This bill is not concerned even remotely with that problem. It is exclusively a matter of State law whether drugs that can be dispensed without a prescription must or must not be sold in drug stores.

This bill in my opinion is clearly in the public interest. It clarifies the law with respect to matters that have brought great concern to practicing druggists. At the same time it makes certain that the public welfare is fully protected. The bill is distinctly beneficial to the general public. It deserves the support of the House.

Mr. CROSSER. Mr. Chairman, I yield 15 minutes to the gentleman from Mississippi [Mr. WILLIAMS].

Mr. WILLIAMS of Mississippi. Mr. Chairman, I wish it were possible for my good friend the gentleman from North Carolina [Mr. DURHAM] to be here today to present the case for this bill. As all of you know, he has been fighting to get the retail druggists out of the dilemma in which they found themselves after Dr. Dunbar's speech to the NARD convention in 1948.

This is the first time we have been able to get his legislation to the floor. The gentleman from North Carolina [Mr. DURHAM], as you know, is in the hospital now, and it is impossible for him to be here. If he were here, I am sure this bill would meet with little, if any, opposition.

As a member of the Committee on Interstate and Foreign Commerce, which considered this legislation, I am one of those who feels he knows a little something about the bill. We have, in committee, gone over all of the objections which have been raised on the floor. There is nothing new in the arguments against the administrative list provided for in this bill. They have all been argued back and forth and ironed out in committee. When the bill was finally put to a vote by the membership of the committee, it was reported favorably to the floor of the House by a vote of 19 to 4.

As you know, the only controversial item in the bill has to do with subparagraph (B) of paragraph (1). That subparagraph, as you know, provides that the Administrator shall, after hearings, and so forth, provide an administrative list of drugs which shall be restricted to sale under prescriptions. That is the bone of contention in this bill.

The amendment which will be offered by the gentleman from Minnesota to strike this language from the bill and substitute therefor what they consider a definitive standard by which the manufacturers may determine which drugs are prescription drugs has been considered at length by the committee. It was voted down by an overwhelming vote, and this language giving the Administrator this responsibility was written in the bill in its stead.

The arguments against putting the administrative list provision in the bill are simply the same old arguments we heard on the floor of the House from time to time when Federal Security matters are considered. I must confess I have at times advanced the same arguments to accomplish my purposes.

The argument against giving any additional authority to Oscar Ewing is powerful and has a tremendous political appeal because of his apparent unpopularity. Do you not know that if this bill gave any additional authority—arbitrary authority—to Mr. Ewing that I would not be here fighting for its passage, and to include the section providing for the establishment of this administrative list? Knowing my record here, do you think I would be fighting to give one of Mr. Truman's Fair Deal bureaucrats arbitrary authority which he could abuse? Do you think I would be here trying to promote socialized medicine? I suspect that my record of fighting Mr. Ewing and his socialistic ideas is just about as consistent as that of the gentleman from Minnesota.

Do you think if there was danger of giving Mr. Ewing dictatorial powers in this bill that the gentleman from Arkansas [Mr. HARRIS] would be here fighting in support of it? Do you think that

the gentleman from Florida [Mr. ROGERS] would be giving the bill his wholehearted support? Do you think the gentleman from Alabama [Mr. ROBERTS], and the gentleman from Texas [Mr. THORNBERRY], all conservatives and all feeling generally as I do about government—and Mr. Ewing's socialistic philosophies—would be supporting this bill? Do not you know that there is no danger of Mr. Ewing's becoming a medical dictator through this bill? We would give him this authority, and then tie his hands with the Administrative Procedure Act so he could not abuse it.

Mr. SABATH. Mr. Chairman, will the gentleman yield?

Mr. WILLIAMS of Mississippi. I yield to the gentleman from Illinois.

Mr. SABATH. This will not be administered by any bureaucrat. It will be administered by a man who has been in civil service for many years. As to the gentlemen who are supporting this bill, I am pleased that they are doing so. I hope that in the future they will continue to support other administration bills as they are doing this time.

Mr. WILLIAMS of Mississippi. I thank you for your help. But I am not going to argue with you whether Mr. Ewing is a bureaucrat or not. Frankly, I would concede that point. This bill gives Mr. Ewing certain responsibilities in subparagraph (B) of paragraph (1), and then ties his hands so that he cannot abuse it. Later on in the bill this is provided through court appeals granted to the objectors.

Mr. HARRIS. Mr. Chairman, will the gentleman yield?

Mr. WILLIAMS of Mississippi. I yield to the gentleman from Arkansas.

Mr. HARRIS. I know the gentleman has a valuable statement to make, and I do not want to take up his time. I hope that every Member will listen attentively to a man who has such a background, raised in a drug store, and is therefore familiar with the problems involved here. With reference to the statements of the distinguished gentleman from Illinois [Mr. SABATH], I should like to say that this is not necessarily an administration bill. It was presented to our committee by the gentleman from North Carolina [Mr. DURHAM] and it is a bill for and in behalf of the people of this country.

Mr. SABATH. To that extent I agree with the gentleman.

Mr. HARRIS. As long as such legislation is in the interest of the people of the country, I can assure you that the Members the gentleman refers to will still be supporting it.

Mr. PASSMAN. Mr. Chairman, will the gentleman yield?

Mr. WILLIAMS of Mississippi. I yield to the gentleman from Louisiana.

Mr. PASSMAN. Under the bill the Federal Administrator can make a determination on the basis of statutory standards and define dangerous drugs, on the basis of generally prevailing administrative opinion. Is the Administrator a doctor or a druggist himself?

Mr. WILLIAMS of Mississippi. He is not; he is the head of the Federal Security Agency.

Mr. PASSMAN. He would not make decisions himself? He would have to seek the advice of others, other than his own decisions?

Mr. WILLIAMS of Mississippi. This authority had to be placed in somebody. Therefore, it was placed in the head of the Agency rather than in one of his subordinates in the food and drug section of his Agency.

Mr. FORD. Mr. Chairman, will the gentleman yield?

Mr. WILLIAMS of Mississippi. I yield to the gentleman from Michigan.

Mr. FORD. I just asked a member of the committee as to whether or not the Federal Security Agency could handle this new assignment if it is given to them, with their existing personnel, or whether they are going to have to come before the House Committee on Appropriations and request additional personnel to handle the new duties, if this bill is approved. Can the gentleman tell me whether or not that was brought out in the hearings?

Mr. WILLIAMS of Mississippi. No, I cannot say, of my own knowledge. I assume they will probably act like nearly every other agency, they will probably come back and ask for some more funds. But I am convinced it could be handled within the present framework of the Agency.

Mr. FORD. That would be an exception to previous experiences Congress has had with reference to new duties being put on Government agencies?

Mr. WILLIAMS of Mississippi. Well, the gentleman knows the habits of these agencies when it comes to asking for their funds. They look for excuses to justify additional funds. But, frankly, this could be handled within the framework of the Agency.

I hope you will now let me continue for a moment without interruption. The commitee, in attempting to place responsibility for determining what drugs are prescription drugs and what drugs are safe to be sold over the counter, considered three alternatives.

First, the committee considered the proposition of writing into the bill a legislative list, naming the drugs which could be used as examples in determining which drugs are prescription drugs.

Of course that is legislatively impossible; we cannot handle legislatively something that should and could only be properly handled administratively, and that idea was set aside.

The second alternative that was presented to the committee was the proposition of including in the bill a legislative standard to be followed by the manufacturers in determining what legend to put on their drug. That is the present law and has caused the presently existing confusion. I see no way of enforcing that. That was considered long and it was considered tediously by the committee, and that, I understand, is what is going to be offered as a substitute for the language of this bill when it is read under the 5-minute rule.

Had the committee written that language into the bill and attempted to provide a broad definition of what drugs should be prescription drugs and what drugs could be sold over the counter, the individual retail pharmacist would be left in exactly the same position he is in now. That is, whether to believe the legend that was written on the drug by the manufacturer that it could be dispensed only under the supervision of a physician, or whether he could freely sell the drug over the counter.

Let us take the case of precipitated chalk that was brought before the committee. One manufacturer put on precipitated chalk the prescription label saying that it cannot be sold except under the supervision of a physician or on the written prescription of a physician. Another manufacturer puts up the identical drug, the same chemical makeup—an innocuous drug, incidentally—puts on the label, not the prescription legend, but the dosage: "One teaspoonful in a glass of water every 2 hours as an antiacid."

What is a druggist going to do when he gets a request from a customer to sell him over the counter an order of precipitated chalk? Does he know whether he can legally sell it? Or does he know whether he is violating the law when he sells it? The purpose of this bill is to give that druggist a definite standard to follow. If this bill is passed within 6 months all the druggist will have to do to be sure whether he is violating the law or not is to look at the legend written on the drug before he dispenses it.

Mr. CROSSER. Mr. Chairman, will the gentleman yield?

Mr. WILLIAMS of Mississippi. I yield.

Mr. CROSSER. As distinguished from the present situation where he has to invite prosecution to find out.

Mr. WILLIAMS of Mississippi. You are right. The present situation is one of confusion, but to adopt the definitive standard amendment would merely place a congressional stamp of approval on the present confusion.

Mr. BATTLE. Mr. Chairman, will the gentleman yield?

Mr. WILLIAMS of Mississippi. I yield.

Mr. BATTLE I want to say that I have had a great deal of correspondence from my retail druggists on this very point and I think they are due some relief. I want to congratulate the committee for bringing out this legislation to clarify these points. I congratulate the gentleman on his statement.

Mr. WILLIAMS of Mississippi. I thank the gentleman.

Mr. BENNETT of Michigan. Mr. Chairman, will the gentleman yield?

Mr. WILLIAMS of Mississippi. Not now.

Mr. BENNETT of Michigan. If the gentleman will yield I just want to clear up a point.

Mr. WILLIAMS of Mississippi. We can argue that point later. I know what the gentleman is going to say; we have discussed that before. The gentleman can take it up when he makes his statement on the floor and I promise him that I will not interrupt his reply.

Mr. Chairman, during the last 2 or 3 weeks when certain drug manufacturers found out that this bill was coming up for consideration they began to spread misleading information all

over the country about the bill. They have told the people that dispense home remedies, such as Watkins and Raleigh products, that they would be put out of business. They have even been telling the little country grocers that they were not even going to be able to sell vanilla extract; that if this bill passed, the only way a person could get vanilla extract would be on the prescription of a physician. Now that, of course, is untrue. It is grossly misleading, it is a fabrication out of the whole cloth, and it is intended to stir up enough grass-roots opposition to this bill, based on a misunderstanding of it, to persuade the membership of this House to refuse this relief to the retail druggists of America.

The CHAIRMAN. The time of the gentleman from Mississippi has expired.

Mr. CROSSER. Mr. Chairman, I yield the gentleman two additional minutes.

Mr WILLIAMS of Mississippi Mr. Chairman, let us see who is supporting this bill. Among the organizations supporting this bill is the National Association of Retail Druggists, which has a membership of 35,000. Practically every drug store owner in the United States belongs to the NARD. This is the real practical working organization of the American retail drug stores. With 35,000 members, that organization is seeking relief for its members.

Who is opposed to this bill? The American Drug Manufacturers Association, with a membership of 67 firms. Are they interested in the welfare of the retail druggist when it conflicts with their own? Self-preservation is still the first law of nature.

Then another is the American Pharmaceutical Manufacturers Association that has a membership including 150 firms. There is the Proprietary Association, composed essentially of manufacturers of what they call packaged medicines or patent medicines. These are the products sold to the general public with representations as to the effects they will produce rather than with emphasis on the ingredients of which they are composed, such as Hadacol for instance.

Then there is the American Pharmaceutical Association you have been so worried about because you have been getting letters and telegrams from them in opposition to this bill. Who is the American Pharmaceutical Association? Does it claim the right to speak for the American retail druggists as opposed to the National Association of Retail Druggists?

The American Pharmaceutical Association represents primarily the scientific side of pharmacy. It represents school teachers, research men, and others who are connected with drug firms, and others interested in the sale of drugs—but not necessarily retail drug stores—and it only has 14,000 members in the organization.

There is the NARD, made up of the retail drug store owners of this country, which is virtually unanimous in support of this bill.

You have 35,000 professional men, practical men, on one side through the NARD. Take a combination of all the rest of them and you do not have over half as many people as you do in the NARD. I am convinced that the retail druggists want and need this bill.

The CHAIRMAN. The time of the gentleman from Mississippi has again expired.

Mr. WOLVERTON. Mr. Chairman, I yield 7 minutes to the gentleman from Indiana [Mr. BEAMER].

Mr. BEAMER. Mr. Chairman, on Monday, in the debate on H. R. 4484 and on many previous occasions many Members of this House have pronounced their affirmation in the sovereignty of the States and in opposition to increased Federal controls. The same principle is involved in a portion of this measure, H. R. 3298. The administrative enmeshment and the grant of great power which H. R. 3298 provides are not necessary to the avowed purposes of the bill.

The principal intent of this bill is to correct and improve the refill provisions of the present pure food and drug law. This result, we feel, has been accomplished in a reasonably good manner in H. R. 3298. However, attention must be called to the section that gives increased authority to the Federal Security Administrator.

Another interesting and important process in legislative procedure is deserving of attention. When the Interstate and Foreign Commerce Committee voted in executive session on this bill several of us wanted this one feature corrected and, for that reason, hoped to have the committee further consider it. Immediately the National Association of Retail Druggists wrote the members of their association in my district, and, I presume, in certain other districts. As a result I received letters from 10 druggists, most of whom I know personally, asking me to support H. R. 3298. Accordingly, I sent copies of the bill and also of the committee report to these retail druggists with a request that they study the bill and the committee report. Time has been limited, but, even so, I have received telegrams from 5 of these druggists in which they reverse their original request and ask me to support only the refill provision and oppose the extension of authority.

In addition, I have received some 45 or 50 other telegrams principally from the doctors in one city in my district in which the same sentiment is expressed that the druggists requested after they had learned for themselves the content of this bill.

These druggists and doctors realize—as do you and I—that the old legislative trickery is being employed. Some more of the socialistic schemes are introduced in this manner by incorporating worthwhile legislation which we want to support with objectionable sections which we must oppose. In this dilemma the druggists who really have had an opportunity to know the actual import of this kind of legislation really are saying that they do not want to sell their birthright for a mess of pottage.

As evidence of the attitude of these druggists once they see the entire picture, I wish to include two telegrams that are typical:

ANDERSON, IND., *July 29, 1951.*

JOHN V. BEAMER,
House of Representatives,
Washington, D. C.:

After conscientious reconsideration of H. R. 3298 in its revised form may I ask that you use your influence in writing in improvements whereby physicians may have the right to prescribe medicines orally, and pharmacists may fill prescriptions so received and refill those and any other prescription he may have on file except those covered by the Federal narcotics laws. That physicians may indicate the number of times the pharmacist may refill each prescription, by noting thereon. That you use all the available pressure at your command to defeat any additional moves by the Administrator of the Social Security Administration to increase his controls over the practice of medicine and pharmacy, and if possible to decrease his control over the practice of medicine and pharmacy, and if possible to decrease these bureaucratic controls. After 40 years of the profession of pharmacist my observations are that pharmacy and medicine need less controls and that the majority of these professional men are honest and honorable and are able to police their own professions.

A. L. PAYNTER.

ANDERSON, IND., *July 29, 1951.*

Hon. JOHN V. BEAMER,
House Office Building:

After careful review of H. R. 3298 and majority and minority report I wish to withdraw my approval of original bill.

We believe refill and oral prescription rights absolutely essential to providing customers and doctors with best care and service. Request you support these provisions. Portion of bill giving administration right and power to determine category of drugs and to regulate same should be vigorously opposed. We have too much bureaucracy and control in such departments. It would be almost impossible to keep up with regulations if this were enacted. Please support refill and oral prescription rights but oppose additional restriction and regulation on pharmacists and public as well as additional power for Administrator.

HOWARD GWINN.

I also wish to introduce in the RECORD, 1 telegram from a doctor that expresses the sentiments of the 45 or 50 telegrams that have been received from doctors in my district:

ANDERSON, IND., *July 30, 1951.*

Representative JOHN V. BEAMER,
House Office Building:

Instructed by my committee to express opposition of Madison County Medical Society to H. R. 3298 as written privilege of refill of prescriptions as specified by physicians in use of oral prescriptions essential to save expense and reduce inconvenience to patient and to prevent unnecessary use of physicians' time. We support refill privilege as specified by practitioner for stated number of times and oral prescription when necessary. Remaining portion of bill would compound confusion, increase Federal power and authority over citizens, expand Federal Bureau, lead to increased Federal spending and eventually lead to Government control of medical practice. We request your opposition to giving Administrator more power. If such control is advisable it should be at State level but this is not necessary. We sincerely request you support refill provision and eliminate control or extension of authority of Federal Bureau.

JOHN L. DORNER, M. D.,
Chairman Committee.

Furthermore, a resolution adopted by the Indiana Pharmaceutical Association in convention in June 1951 is included. This resolution further bears out the same opposition to increased Federal controls:

RESOLUTION OF INDIANA PHARMACEUTICAL ASSOCIATION CONVENTION, JUNE 1951

Whereas there is so much disagreement over the right of the registered pharmacist to refill prescriptions of physicians, dentists, or veterinarians for hypnotic and prescription legend drugs: Therefore be it

Resolved, That the Indiana Pharmaceutical Association in annual convention assembled oppose the extension of Federal control over the relationship between physicians, pharmacists, and patients; and be it further

Resolved, That we recommend that such questions as refills of prescriptions be controlled at the local or State level.

A final and very significantly important letter to be included is the one received from Glenn L. Jenkins, dean of the school of pharmacy, Purdue University, West Lafayette, Ind. Dean Jenkins is recognized as one of the outstanding authorities in his field:

PURDUE UNIVERSITY,
SCHOOL OF PHARMACY,
LaFayette, Ind., July 20, 1951.

Hon. JOHN V. BEAMER,
Congress of the United States,
House of Representatives,
Washington, D. C.

DEAR CONGRESSMAN BEAMER: I am pleased to have your letter of July 11 asking my opinion relative to the Durham-Humphrey bill. In my opinion this bill would take away much of the professional liberty of the pharmacist and would interfere with the relationship between the physician and the pharmacist. Furthermore, the bill gives authority to the Food and Drug Administration to determine when a drug is effective. Broad powers of this kind might very easily interfere with the proper self-medication for minor symptoms and ailments carried on by the people. Consequently, it is my opinion that the Durham-Humphrey bill, H. R. 3298, should not be approved by the Congress of the United States. It is my opinion that the control of relationship between the physician, the pharmacist and the patient should be carried out at the State level. A recommendation to this effect was recently passed by the Indiana State Pharmaceutical Association in its annual convention. Consequently, I hope that you will use your efforts to defeat this new legislation.

Sincerely yours,
GLENN L. JENKINS, *Dean.*

There are several underlying principles involved in this measure. One is the fact that oftentimes blind support is given to legislation by well meaning citizens who have been urged by some association executive to contact their Congressman. Once these same people learn the entire contents of the measure, they then realize that the total sum of the dangers involved more than offset the advantages. This fact has been exemplified in this instance.

The other principle which we must repeat time and time again is the fact that all authority dare not be vested in these bureaus in Washington. Indiana and all of the other States of this great Republic have sovereign rights not only in property but also in individual freedoms. There are those who would destroy this principle by chipping away piece by piece this foundation of individual freedom and individual responsibility.

The Federal Wood, Drug and Cosmetic Act has embodied, in the main, this principle and this sound philosophy that has given it strength and respect since the date of its enactment.

With proper amendment to H. R. 3298, this principle can be preserved and, at the same time, the retail druggists, the doctors, and the general public can be given the relief of the prescription refill provisions to which they are entitled.

Mr. SHAFER. Mr. Chairman, I ask unanimous consent to extend my remarks at this point in the RECORD.

The CHAIRMAN. Is there objection to the request of the gentleman from Michigan?

There was no objection.

Mr. SHAFER. Mr. Chairman, I concur fully with the minority report on H. R. 3298, the bill to amend section 503 (b) of the Federal Food, Drug, and Cosmetic Act.

I see no objections to the provisions of the bill governing the filling or refilling of oral or telephone prescriptions, and restricting the refilling of prescriptions dispensing dangerous drugs, except when authorized orally or in writing by the physician.

But I am completely opposed to the remaining provisions of the bill, which would delegate to the Federal Security Administrator authority to determine the category in which each of some 30,000 drugs would be placed, with respect to their sale by prescription only or over the counter.

I strongly oppose this provision on three counts:

First of all, it represents one more in the long sequence of attempts, successful in all too many instances, to merge the legislative, administrative, and judicial functions of Federal Government in a bureau or agency of the executive department. By conferring authority to determine the category in which each of some 30,000 drugs would be placed, we bestow on FSA, on Mr. Oscar Ewing, and on his successors as Federal Security Administrator, the power to legislate by directive. Obviously, the bill entrusts the administration of the provisions of the bill and the provisions of the Administrator's directives to the FSA. Finally, since the bill provides that "the findings of the Administrator as to the facts, if supported by substantial evidence, shall be conclusive," the Administrator's powers become judicial as well as legislative and administrative. This is the familiar story of concentration of power through the merger of powers and the elimination of checks and balances. I oppose it, in principle and in application.

In the second place, this provision follows the customary pattern of power-grasping bureaucracy, by undertaking detailed supervision instead of providing broad, statutory definitions and regulations directed at the source of the problem. Thus, this provision is not content to set up a statutory standard to guide and direct the determination whether a specific drug is to be restricted to sale on prescription. This provision is not content to impose such a standard at the source of original production and distribution—the drug manufacturer—with final determination left to the courts, in case of alleged violation.

Bureaucracy must always do it the hard way, the complicated way, the red-tape way, the costly way, the burdensome way, the way that provides more Federal jobs, more bureaucratic authority.

The detailed decisions as to the category in which each drug is to be placed would, under this provision, be exercised by the Federal Security Administrator. The directives are to go to each druggist. So are the interminable revisions of regulations. The heavy hand of the bureaucrat is to be laid, in one more respect, on the small-business man.

The reasoning of bureaucracy is inescapable and frustrating—even if illogical; why do the job the simpler way, the less expensive way, the obvious way, even though this simpler way will do the job as well or better? The answer is not difficult: The simpler way involves less power for those whose passion is to govern.

Finally, I oppose this proposal because, as the minority report so ably points out, this provision may easily become the handmaiden to socialized medicine. Mr. Ewing's predictions on the score are too well known to require elaboration. As the minority report points out, the provision involves potentially "in time, an over-all control of the manufacture, distribution, and administration of drugs." Added to that is the fact that this provision gives the Federal Security Administrator opportunity increasingly to restrict over-the-counter sale of drugs, thereby increasing cost of medication and creating one more artificial stimulus to the demand for socialized medicine.

There is a legitimate function, and a legitimate method, of safeguarding the public in the matter of production and dispensing of drugs.

But there are always those—as in this case—who seize upon this legitimate function, and distort the legitimate method, to dispense the deadlier drug of centralized and entrenched bureaucracy.

Mr. WOLVERTON. Mr. Chairman, I yield 12 minutes to the gentleman from Minnesota [Mr. O'HARA].

Mr. O'HARA. Mr. Chairman, I appreciate the sense of confusion as to the effect of the statements which have been made here today in this debate. I wish you could imagine the state of confusion in the committee when the original Humphrey-Durham bill was before us and we found the doctors opposed to it and the retail druggists for it, and the pharmaceutical associations and the various drug manufacturers against it. But that bill was not as bitterly opposed as what finally was the child which was born and which has been presented to the floor, which was a very drastic change in the so-called Durham bill. I have received letters calling attention to the fact that it was the Humphrey-Durham bill, so I assume they were both druggists.

There grew up some controversy yesterday as to what the position of the American Medical Association was on this bill. So that there will be no question about it, I should like to read a telegram I received this morning, which is as follows:

In light of the discussion on the floor on H. R. 3298 as to the position of the American Medical Association, let me advise that on recommendation of the legislative committee, the board of trustees authorized opposition to the bill particularly because of section (B). The board of trustees is the policy-forming body of the American Medical Association when the house of delegates is not in session and has been specially authorized by it to take action on legislative bills. Action on H. R. 3298 was taken by the board at a meeting June 14, 1951, and a copy immediately sent to a member of your committee.

I might say that the hearings on this bill were concluded in the early part of May 1951.

That advice was communicated to my distinguished friend the gentleman from Tennessee [Mr. PRIEST], who read the communication to the committee in executive session. Therefore it cannot be claimed that the committee did not know what the attitude of the American Medical Association was on this bill. I enclose copy of this letter:

AMERICAN MEDICAL ASSOCIATION,
Washington, D. C., June 15, 1951.

Hon. J. PERCY PRIEST,
House of Representatives,
Washington, D. C.

MY DEAR CONGRESSMAN PRIEST: The legislative committee of the American Medical Association has given a lot of thought and study to H. R. 3298, the Durham drug bill.

The provisions of the bill were especially studied by our council on pharmacy and chemistry, and the following statement has been prepared and is being submitted by the board of trustees.

"The committee believes that the objectives sought by this legislation are worthy of support but legislation as proposed at the present time is not necessary or desirable. The committee also believes the control of professional practices should remain in the bodies already set up in States to regulate professional practice. The determination of what should be labeled only for prescription use and what should be made available for nonprescription dispensing should be left to voluntary discussion and effort as now possible under the Federal Food, Drug and Cosmetic Act. The Committee therefore disapproves the legislation."

Respectfully submitted.

JOS. S. LAWRENCE, M. D.,
Director, Washington Office.

Mr. CROSSER. Mr. Chairman, will the gentleman yield?

Mr. O'HARA. I yield.

Mr. CROSSER. The gentleman does not mean to say that the American Medical Association responded to the usual notice which was sent out to the usual organizations and institutions that such notices are sent out to when hearings are going to be held.

Mr. O'HARA. I did not say that, may I say to my Chairman.

Mr. CROSSER. As a matter of fact I personally met the representative here in Washington and asked him whether his organization was going to take a position and I was pretty well informed that it was not going to take a position on this.

Mr. WILLIAMS of Mississippi. Mr. Chairman, will the gentleman yield?

Mr. O'HARA. I yield.

Mr. WILLIAMS of Mississippi. The gentleman knows that we did everything but hogtie the doctors to try to get them down before the committee.

Mr. CROSSER. Absolutely.

Mr. WILLIAMS of Mississippi. And they absolutely refused to take a stand.

Mr. O'HARA. The gentleman knows that some doctor who represents the American Medical Association in Washington cannot speak until the executive board of their body acts on any particular project. Until the bill came out of committee they could not possibly have acted on it and furthermore when the bill was reported out of committee it was completely changed. I say in fairness to the American Medical Association they have been a little slow in reporting their attitude at times and I have been critical of them but in this case I cannot criticize them.

Mr. BROWN of Ohio. Mr. Chairman, will the gentleman yield?

Mr. O'HARA. I yield.

Mr. BROWN of Ohio. I have had the opportunity, of course, to hear a great deal of discussion on this bill before the Committee on Rules. I have received a great many communications from druggists, a few from drug manufacturers, and a large number from doctors, from all over the country concerning this legislation. I have sent copies of the bill and of the committee report to those people who contacted me, especially those in my own district and State. I know that the Ohio State Medical Association, for instance, has gone on record against the provisions in the bill which gives greater power to the Federal Security Administrator. Seemingly the druggists are primarily interested in getting the authority to refill prescriptions so as to follow their age-old custom of handling prescriptions, while the doctors are primarily interested in seeing that no one gets a foot in the door for socialized medicine, and are therefore opposed to the section giving new powers to FSA. The doctors and the medical fraternity, as I understand it, also want the relief the druggists have requested to be granted to them. So it seems to me we can work out a suitable arrangement to satisfy both doctors and druggists by amending this bill, so as to give to the druggists the relief they seek, and at the same time to protect the medical profession from the threat of socialized medicine.

Mr. O'HARA. May I say, Mr. Chairman, that I intend to offer an amendment which will strike out the objectionable features of this bill, namely, amending B and striking out subsection 5. That will remove this tremendous grant of administrative absolutism to Mr. Ewing as the Food and Drug Administrator, and I am sure a great many Members and many, many of the people of this country do not want him to have such power.

You have a sugar-coated pill here. The question which came before us was the chaos created by the Dunbar speech at Atlantic City in 1948 when the traditional oral prescription was removed and the refilling of the prescriptions was eliminated. There was never an official ruling made by Food and Drug; just a speech by Dr. Dunbar, of the Food and Drug Administration, telling them how wrong it was. Everybody is for legislation that will clear that up.

But when they got that far, in comes the Food and Drug Administration and hang on a tremendous grant of power, which gives Mr. Ewing authority, from the traditional case-by-case decision, which he has today, to making 30,000 decisions at once or in doses of 500 or in doses of 100, and the retail druggists from then on are supposed to keep up with what goes on.

Here is another thing that it does: In the practice which exists today the druggist has the defense of good faith when he buys drugs from a drug manufacturer. Usually there is a guaranty on the bill of sale, or whatever passes from the drug manufacturer to him. It is a recognized fact that the retail druggist has that defense of good faith. I say this to you who are for the National Association of Retail Druggists—you can ask any lawyer what it means—the druggist is now eliminated from this defense of good faith under the language of this bill, and he is on his own.

There is another thing that the druggists of the country do not know what is happening to them. That is, if there are a large number, and I assume there will be, of these decisions on various items of drugs, it is going to be up to the druggist to see that he takes care of the labeling on his shelves. He is going to have to see from day to day what Mr. Ewing has passed out in the way of regulations, change the prescription drug to an over-the-counter drug, or an over-the-counter drug to a prescription drug. Now, let there be no question about that.

Mr. SPRINGER. Mr. Chairman, will the gentleman yield?

Mr. O'HARA. I yield to the gentleman from Illinois.

Mr. SPRINGER. By your amendment you will strike out section 5; is that true?

Mr. O'HARA. Yes.

Mr. SPRINGER. Will there be any substitute for section 5?

Mr. O'HARA. I do not know.

Mr. SPRINGER. With reference to the question of the right to judicial review——

Mr. O'HARA. Let me say to the gentleman that if the section is stricken out the judicial review is eliminated. You do not have to worry about that.

Mr. SPRINGER. That is what I wanted to be sure about. You are not going to have any problem of following decisions.

Mr. O'HARA. You have got these six or eight steps under this bill that the person affected would have to go through. When you get down to the end of it you have very little judicial review.

Mr. SPRINGER. By your amendment, what will it do?

Mr. O'HARA. It will amend subsection (B) and clarify it. I do not know what that will mean if it is not adopted in its entirety. It will mean that it will make it very simple and clear as to what the Administrator is to do in making

these tests. My amendment will then strike out subsection (5), which is the grant of power to the Administrator. He does not have to give anybody a hearing to make these decisions, and unless they object or petition for a hearing upon that previous decision. Now, that puts the burden of proof on the other foot, instead of as it is today. The burden of proof is reasonably upon the Administrator when he comes into court to enforce the authority which he has now. There is no question but that the Administrator has all the power in the world now. If a drug is mislabeled or misbranded or not approved as it should be for sale to the public, the Administrator has all the authority in the world to bring prosecution, either criminal prosection, or to seize it under a libel, and prosecute that action.

Mr. SPRINGER. Now, the third question: Under your amendment, will your definition be complete enough that these country stores and others who are now selling proprietary medicines can continue to do so in the same manner that they do now?

Mr. O'HARA. Yes; there is no question about that; he would still have the decision to make as to whether it was something that should be sold; he has that today.

Mr. DONDERO. Mr. Chairman, will the gentleman yield?

Mr. O'HARA. I yield.

Mr. DONDERO. If the gentleman's amendment should be adopted, would the ordinary person be able to have his prescriptions filled with the same ease with which he can do so today?

Mr. O'HARA. Yes; exactly; and without all of this other mess which is going to be confusing to everybody involved in the drug business.

Mr. DONDERO. Then what was the basis—and I do not ask the gentleman to repeat the statement he has already made—what was the basis of bringing this legislation to the floor of the House?

Mr. O'HARA. That was one of the strange things that my friends on the other side, on the right side of the aisle, are still apologizing for.

Mr. CRAWFORD. Mr. Chairman, will the gentleman yield?

Mr. O'HARA. I yield.

Mr. CRAWFORD. The bill was brought in by two professional pharmacists, was it not?

Mr. O'HARA. That is what I assume.

Mr. CRAWFORD. So there may be no doubt about it, it is a bill in favor of a special interest, the druggists.

Mr. GWINN. Mr. Chairman, will the gentleman yield?

Mr. O'HARA. I yield.

Mr. GWINN. Would not this be an intolerable and objectionable thing for the doctors if every time a person wanted Mothersill's seasick pills he had to go to his doctor?

Mr. O'HARA. And get a prescription.

Mr. GWINN. And get a prescription. Is not that right?

Mr. O'HARA. That is what could happen; and they say that even aspirin could be included, as a prescription drug.

Mr. CROSSER. Mr. Chairman, I yield 10 minutes to the gentleman from North Carolina [Mr. CARLYLE].

Mr. CARLYLE. Mr. Chairman——

Mr. WILLIAMS of Mississippi. Mr. Chairman, will the gentleman yield?

Mr. CARLYLE. I gladly yield to my friend from Mississippi.

Mr. WILLIAMS of Mississippi. The gentleman knows that they would never be able to put Mothersill's seasick pills or Lydia Pinkham's pink pills or Hadacol, or other such patent medicines on the prescription list under the definition mentioned in this bill.

Mr. CARLYLE. Mr. Chairman, I welcome this opportunity to make a few brief statements in support of this highly important and wholesome legislation.

Mr. Chairman, I would be unmindful of my duty should I fail to state that our able, experienced, and efficient chairman realized the importance of this legislation and he gave every interested party who expressed any desire to testify before our committee the opportunity to do so. I know of no person or corporation that has requested the opportunity to appear before our committee who was not afforded that opportunity.

This bill we are now considering is not based upon theory or conjecture; it is based upon actual experience of the druggists in this country. We know that the author of this bill is a Member of Congress and is at all times a dependable Member. I have known the gentleman from North Carolina [Mr. DURHAM] for more than 30 years. I know that he was a successful operator of a drug store and is now a skilled, successful, and highly efficient registered pharmacist in the State of North Carolina. Based upon his experience and upon his desire to be of assistance to the people of this country, he introduced this legislation.

I wish to state that my primary interest in this legislation is because I know that it is wholesome, that it is needed in this country in order to prevent gross injustice and to cure many evils that now exist. When you take into consideration that your action here today regarding this bill will vitally affect every home and every person in this country at some future date, you can readily see why you should give your best thought and consideration to this bill. Now, personally, I see no possible opportunity for one to become confused while considering this bill. There is no confusion in my mind.

The bill contains three separate provisions, and I ask you in your mind to answer which one you cannot wholeheartedly embrace. One section provides that a doctor shall have the right, if he thinks it is necessary, to transmit his prescription to the druggist by telephone. Of course, then the prescription druggist will make a copy of that prescription and file it. Probably thousands of instances occur in this country every day where a physician is called to a home or to the scene of an accident for the purpose of rendering services. When he there finds a prescription medicine is necessary, he may use a telephone to communicate with the druggist and the medicine is forthcoming. That is a violation of law in this country, both on the part of the physician and the druggist. One provision of this act expressly provides that condition shall be corrected and a doctor may have his prescription filled by transmitting it to the druggist by telephone. You know that is a wholesome provision in this bill.

There is another provision that I ask you to consider and to which I wish to invite your attention. If you desire to have a prescription refilled and harmful medicine is not required, then you may carry your prescription or carry your bottle to the druggist and this law will permit the druggist to refill your prescription provided the original prescription did not contain the statement by the doctor that it could not be refilled. You know that will prevent much confusion and loss of time and money on the part of the patient. This provision of the bill makes it easier for the patient to obtain a refill without having to obtain another prescription. Is there anything objectionable to that provision of this bill?

Now, the third provision which I ask you to consider is simply this: We know there are many drugs now being dispensed in this country that are in what we call the harmful classification. Harmful drugs may, in order that the public may receive proper attention, be dispensed only upon a doctor's prescription. There are other drugs that are not considered harmful that may be sold across the counter without a doctor's prescription. But within those two groups of drugs that have just been mentioned, harmful and harmless, there is a zone that is doubtful, and it gives the druggist considerable trouble to know at all times just which drug is harmful and which is not harmful. I say to you that the druggists throughout this country have figuratively speaking been swinging on the jail house door, because they are called upon in the course of their business to dispense drugs, many of them within the twilight zone, and the druggist oftentimes is unable to know whether he is violating the law by selling a drug that perhaps could be classified as harmful, without a prescription, and thus, of course, he would be violating the law.

Mr. BECKWORTH. Mr. Chairman, will the gentleman yield?

Mr. CARLYLE. I yield to my friend the gentleman from Texas.

Mr. BECKWORTH. The gentleman has made a very excellent point. The gentleman has heard the gentleman from Minnesota [Mr. O'HARA] say he is going to offer an amendment. Does the amendment he proposes to offer have any bearing on the correction the gentleman says should be brought about right there?

Mr. CARLYLE. I hope I shall have time to answer the gentleman before I conclude.

Mr. BECKWORTH. I am talking about the O'Hara amendment. Does the

gentleman know whether it has any bearing on that which he is talking about in the twilight zone?

Mr. CARLYLE. I tell the gentleman frankly, in answer to his question, I know of but one way to protect the American public and the druggist and that is to furnish the druggists throughout this country a list that will enable them to have some guide, some direction, which will assist them in making the decision as to whether it is harmful or whether it is not harmful.

Mr. HARRIS. Mr. Chairman, will the gentleman yield?

Mr. CARLYLE. I gladly yield to the gentleman from Arkansas.

Mr. HARRIS. Is it not a fact that if the amendment that is proposed by our colleague on the committee, the gentleman from Minnesota [Mr. O'HARA], is adopted, it would eliminate altogether the efforts to do something about this confusion?

Mr. CARLYLE. I would certainly think so.

Mr. BECKWORTH. Mr. Chairman, if the gentleman will yield further, is there any part of the legislation that the druggists, who seem interested in this bill, seem to want more than the gentleman is talking about?

Mr. CARLYLE. I agree with my friend from Texas. In conclusion, let me insist that we give to our druggists, who are located throughout all sections of this country, the protection that they are now asking for. Give them the right to have some assistance so that they may know that they are not dispensing harmful drugs. This is important legislation. I stated at the beginning of this statement that it touches every home and every person in this country. Let us be positive that we will be guided only to the end that we may afford the best possible protection to the druggists and to the people of this country.

Mr. WOLVERTON. Mr. Chairman, I yield 8 minutes to the gentleman from Michigan [Mr. BENNETT].

Mr. BENNETT of Michigan. Mr. Chairman, I would like to refer to some of the inconsistencies that have been brought into this debate. Some clarification is highly desirable at this point.

Three classes of drugs are covered by this bill. One is the habit-forming or narcotic type of drug. Nobody has any objection to the Federal Security Administrator having all the power in the world to control that type of drug. He has it now. It is being strengthened by this bill, and we have no objection to it. The next category is the new drug, and that has been entirely omitted in this debate. Under present law before a manufacturer can put a new drug on the market he has to go to the Federal Security Administrator and get permission to do it. The label that goes on that drug and whether or not it is a prescription or nonprescription drug has to be approved by the Federal Security Administrator. We do not have any objection to that procedure. That takes care of this new field, this new type of drug, that comes on the market, which may be dangerous, and ofttimes is, and we think that the Federal Security Administrator should have that power.

But what does this bill do? It goes much further. It gives to the Federal Security Administrator authority to classify some 30,000 other drugs that are on the market now, and many of them have been on the market for the last 50 years. There is where we part company with those who sponsored this bill.

There are less than 100 admittedly dangerous drugs being dispensed today. We are providing in this bill authority for the Federal Security Administrator to regulate 30,000 drugs. If he is not going to go into the field of drugs that are now on a nonprescription basis, why does he want this authority? There is no reason in the world for giving him this authority except on the basis that he will use it to take drugs that have been traditionally sold over the counter in the drug stores and in the country grocery stores around this country and put them on the prescription list. If he does not intend to do that, why is he asking Congress for authority to do it?

That is the sum and substance of this legislation. It is not a question of Oscar Ewing or a question of any other administrator. In my judgment, it is a question of whether Congress should delegate this kind of authority to any administrative agency.

What is the situation today? Under present law, the Federal Security Administrator can proceed against any drug manufacturer who he believes is putting out a dangerous drug without a prescription. He can take him into court and prosecute him. He can confiscate the drug. He can proceed against him by injunction. He has several remedies that he can pursue, all of which are effective, and all are in accordance with the standards set up in the law.

What would this bill do? It would simply enable the Administrator to prosecute the druggist or prosecute the drug manufacturer on the basis of regulations which he issues. Not on the basis of the standards set up in the law because, under the provision we are considering, we are giving the Administrator practically autocratic authority to issue these regulations.

This is what will happen. There are thousands of drugs as to which there is considerable difference of opinion, drugs that are being dispensed over the counter today. All the Administrator has to do to put an over-the-counter drug, a nonprescription drug, on the prescription list, is this: He calls in two or three of his medical experts. Everybody knows you can get medical experts to testify on both sides of any question. On the basis of the advice of his own medical experts, he can take a perfectly harmless drug or a drug that for years has been on the market and put it on the prescription list.

Mr. CRAWFORD. Mr. Chairman, will the gentleman yield?

Mr. BENNETT of Michigan. I yield to the gentleman from Michigan.

Mr. CRAWFORD. The gentleman started to make a point about what the Administrator could do with respect to harmless drug which have been sold for many years across the counter. He did not make that point. What can the Administrator do about it?

Mr. BENNETT of Michigan. The point is that the bill gives the Administrator complete and final authority to determine what is a dangerous or efficacious drug and what is not.

Mr. CRAWFORD. He does that with his own staff?

Mr. BENNETT of Michigan. In order to determine that, he calls in his own experts. Of course, the manufacturer of the drugs would call in his experts. So you would have three or four experts of the Administrator and three or four experts from the industry. Then the Administrator would make his decision, and of course he would make it on what his own experts said. The right of appeal which is provided here is a mere sham. It is a nullity. The Administrator has evidence upon which to support his finding and the court is powerless to do anything about it. It all boils down to the question of whether you want to fix the standards in the law. We have been willing to take the regulation which the Administrator has had on the books for some years; the regulation which he is proceeding under today, and in substance write that regulation into this bill. Therefore the question of whether a drug is dangerous or not can be decided by a standard written in a statute and when a drug manufacturer or a druggist appeals his case he will have his day in court. Whereas, under this provision, he does not have his day in court and he is simply out of luck.

It is said that this bill will be a boon to the retail druggist. There are many things the retail druggist does not understand about this bill. If this goes into effect there will be thousands of regulations issued by the Administrator listing these drugs. That means the corner druggist will have to get a copy of the Federal Register containing the list of those thousands of drugs and go over his entire inventory item by item and relabel them to conform with any changes made by the Federal Security Administrator. Do you think the corner druggist is going to like that kind of burden. But his troubles only start at that point. Each day thereafter and each week and each month thereafter he will have to refer to the regulations issued by the Federal Security Administrator, to know whether he is on the right track. The druggist is not going to have any additional protection. That is pure baloney. He cannot rely upon the label that is put on by the manufacturer. It is the regulation of the Federal Security Administrator that he must rely on. After this bill goes into effect, before a druggist can sell a single item on his shelf he must refer to this stack of regulations day by day. Do you not think that we have penalized the small-business man enough with OPS regulations and other governmental regulations being inflicted on him from day to day without handing him another package of this kind to swallow? I think

we ought to stop and give this proposal further thought.

The doctor, the druggist, and the pharmacist, none of whom agree as to how this problem should be settled, but all of whom are vitally affected, should know that there are many dangers involved. This bill should go back to the Committee on Interstate and Foreign Commerce for further study and consideration.

The CHAIRMAN. The time of the gentleman has expired.

Mr. CROSSER. Mr. Chairman, I yield 5 minutes to the gentleman from Alabama [Mr. ROBERTS].

Mr. ROBERTS. Mr. Chairman, I want to discuss the difference between the minority viewpoint and the viewpoint being sustained by the majority members of this committee.

Mr. WILLIAMS of Mississippi. Mr. Chairman, will the gentleman yield?

Mr. ROBERTS. I yield.

Mr. WILLIAMS of Mississippi. I wish the gentleman would state that the minority viewpoint is a minority of 4 of some 12 or 15 members of the minority.

Mr. ROBERTS. I thank the gentleman for his statement. The only difference in these viewpoints is that the minority insists on the proposition that there should be on an appeal from the hearing held under the Administrative Procedures Act a trial de novo in the district court. We considered that proposition in our committee and discussed it thoroughly.

I would like to address myself to the minority viewpoint as expressed by the gentleman from Minnesota. We had Judge Harold Stephens appear before our committee and we listened with interest to what he had to say. They brought up a figure of 30,000 drugs which were to be decided in this listing procedure. I do not know where they got the figure, but I am willing to accept it and make no objection to it. With about 94 district courts in this country, and with manufacturers located all over this United States and the Territories, how in the world could you possibly get any uniformity in these decisions?

They accuse us today of attempting to give a bureaucratic group a great deal of additional power. Let me say this: Mr. Ewing is Administrator of three of our governmental Bureaus—the Public Health Service, Social Security Administration, and the Pure Food and Drug Administration. In carrying out the purposes of this act he is bound to be governed by the advice of experts, scientists, and chemists and men in the Pure Food and Drug Administration. As far back as I can remember they have had the power, as far as narcotics is concerned. We are not asking here for anything that is not already in our Government.

Let me point out to you a few examples. We have had administrative procedure before in the early days of our Government, in the Patent Office. It is also true in the Veterans' Administration, the United States Employees Compensation Bureau, the Social Security Board, the Railroad Retirement Board, the Internal Revenue Bureau, the Board of Tax Appeals, and the Selective Service Administration. All of those operate under the Administrative Procedures Act, and, as far as I have been able to find out, appeals from those decisions are made in exactly the same manner that we ask for in this present bill.

Mr. WILLIAMS of Mississippi. Is it not also a fact that the gentleman from Minnesota [Mr. O'HARA], who is opposing the granting of this authority to an administrative bureau, has the same authority and system of procedure in the fur bill which was passed in this House?

Mr. O'HARA. Mr. Chairman, will the gentleman yield?

Mr. ROBERTS. I yield to the gentleman from Minnesota.

Mr. O'HARA. My fur labeling bill was to correct rackets. This bill will create one, in my opinion. That is why I am consistent about it.

Mr. HARRIS. Mr. Chairman, will the gentleman yield?

Mr. ROBERTS. I yield to the gentleman from Arkansas.

Mr. HARRIS. The gentleman does admit that the same procedure is in both bills?

Mr. O'HARA. No; I do not admit it is the same procedure.

Mr. ROBERTS. I will say this to the gentleman: His bill prescribes that the Federal Trade Commission make up a list of furs. They make up a list of regulations and the only appeal in your act would be this type of appeal.

Mr. O'HARA. We did not prescribe for any list. We compelled the fur manufacturer and the fur seller to put on the fur coat what it was—rabbit or ermine or mink or whatever it was.

Mr. ROBERTS. Well, does the gentleman admit that he did give power to a bureaucrat under this bill?

Mr. HALLECK. Mr. Chairman, will the gentleman yield?

Mr. ROBERTS. I yield.

Mr. HALLECK. The Pure Food and Drug Act, under the requirements of the Labeling Act, the manufacturer must put on the label what he is selling.

Mr. ROBERTS. That is exactly what we are trying to do in this bill today.

The CHAIRMAN. The time of the gentleman from Alabama has expired.

Mr. CROSSER. Mr. Chairman, I yield the gentleman one additional minute.

Mr. BECKWORTH. Mr. Chairman, will the gentleman yield?

Mr. ROBERTS. I yield to the gentleman from Texas.

Mr. BECKWORTH. The gentleman has just made the statement that the manufacturer of drugs places on the package what the package is. One of the things that has the druggists throughout the Nation disturbed is the fact that the same thing is labeled two ways, and each is different. This bill has for its purpose the making of an uncertain situation in that connection, which exists in thousands of cases, a certain situation.

Mr. ROBERTS. The gentleman is eminently correct, and what we are trying to do in this bill is to nail down the authority somewhere—and the druggists want it nailed down. It reminds me of the old story about the mice holding a convention because the cat was catching too many of them. They agreed that something should be done, that a bell should be put around the cat's neck so they would know of its approach. The trouble was that they could not get any of the mice to put the bell around the cat's neck. They want the cat belled, and it is up to Congress to give the druggists some relief. The druggists of this country want this thing nailed down so they will not be slammed in jail, and that is what we are trying to do in this bill.

The argument is made by the gentleman from Minnesota that the review provided in the bill as approved by the committee is too narrow, and deprives the litigants or parties of their day in Court. To agree with him would be to destroy the benefits that this act seeks to provide. It is estimated in the minority report that there are some 30,000 drug items to be classified. Can you imagine the confusion and delay that would result if each one of these was to result in a trial de novo? I think one of the witnesses from the Food and Drug Administration estimated that it would take 10 years to settle these cases. And I think he was an optimist. There are ample precedents for establishing a list by regulations. Our own Government has since the adoption of the first Federal Food and Drug Act in 1906 done so. Many of the States list these drugs by statute, and Canada does so by regulation.

In a letter from the Honorable Henry P. Chandler to the Honorable ROBERT CROSSER, dated March 29, 1951, this statement is made—pages 6 and 7 of the hearings:

> I would point out that the provision that appeals from the order of the Administrator shall be in the nature of a trial de novo, reverses what has been for 20 years or more a uniform trend in the Federal Government to provide for the hearing and decision of appeals from orders of administrative agencies by the courts of appeals upon the record made before the agencies. This procedure has been repeatedly provided for by the Congress, most recently by a law passed at the end of the Eighty-First Congress and approved December 29, 1950 in relation to the review of certain orders of the Federal Communications Commission, the Secretary of Agriculture, and the United States Maritime Commission (Public Law 901, 81st Cong.)

Those who are opposed to the power given to the Administrator suggest a case-by-case settlement of the dangerous drugs and new drugs. The implications and dangers of such a policy are readily apparent. I would like to call your attention to the arguments put forth in the majority report contained on page 10:

First. First the administrative decisions will involve only the drug manufacturers, those who are primarily interested. It would not involve the retail druggists whose only interest is to obtain certainty as to how they may sell given drug.

Second. The duty of determining what is a prescription drug is, by its nature a legislative or rule-making function, unsuited for solution, solely through the judicial process.

Third. The authority is entirely consistent with the action of the Congress in 1938 when the Administrator was given the authority to list habit-forming derivatives of the drugs named in section 502 (d), and it has not been suggested

that this authority has been abused. Attention is further directed to the fact that many States so list by regulation, and the Dominion of Canada.

Fourth. The judicial review provisions afford adequate protection against arbitrary and unjustified action on the part of the Administrator.

Fifth. The proposal of the drug manufacturers that the listing proceed on the case-by-case basis would result in great confusion. Manufacturers situated in different locations and proceeding in different district courts would obtain different results adding up to general confusion. There are more than 80 Federal district courts. With or without juries no uniformity could be obtained.

Sixth. Delay that would result would be injurious to the general public. The sex hormone case took 2 years to settle.

Mr. WOLVERTON. Mr. Chairman, I yield the balance of my time to the gentleman from Maine [Mr. HALE].

Mr. HALE. Mr. Chairman, this bill, as I think most of the Members now realize, represents a very sincere, conscientious, and rather arduous attempt on the part of the Committee on Interstate and Foreign Commerce to cope with very serious problems in the dispensing of drugs.

The three problems which presented themselves to the committee were: First, that of the oral prescriptions; second, that of the refill, so-called; and third, that of the matter of dispensing dangerous and habit-forming drugs. All of these questions concern the responsibilities and hazards of the druggist. They also concern the safety and convenience of the drug-buying public. The committee tried to give due regard to the welfare of the druggist and the consumer. They also listened at length to testimony of drug manufacturers.

I should have thought in my innocence that there was a good deal to be said for the rule against any kind of oral prescription on the ground that oral prescriptions are subject to misunderstanding, but the unanimous testimony of the drug industry, of the druggists, the drug manufacturers, and everybody who came before our committee was that oral prescriptions should be permitted.

Much of the trouble about refills came from the speech made by Mr. Paul Dunbar at a convention in Atlantic City in 1948 when he said that the prescription, once it had been filled, was like a paid and canceled check; it had lost all its force, all its validity, and you had to go back to the doctor to bring such a prescription back to life.

Mr. NICHOLSON. Mr. Chairman, will the gentleman yield?

Mr. HALE. I yield.

Mr. NICHOLSON. Was that the reason they made it so that anybody who wanted another prescription had to pay another $3 to the doctor?

Mr. HALE. That is the kind of thing we are trying to avoid in this bill. I think the bill offers a very adequate and satisfactory solution of the problem of the oral prescription, and the problem of the refill. All the controversy comes over the provisions protecting the public and protecting the druggist in the case of the dangerous and habit-forming drugs.

I was in the minority in the committee; I was one of four who voted for the form of bill which the American Drug Manufacturers advocated that gives no administrative discretion to the Federal Security Administrator to list dangerous and habit-forming drugs. If you do not put that provision in the bill, to be sure, you will have the druggist in a state of some uncertainty, which is what the majority members of the committee were worried about. On the other hand, that uncertainty does not seem to me to be too serious because, if a druggist is worried as to whether a drug he is selling is dangerous and habit forming, he can refuse to sell it without prescription and thus keep himself in a position of safety.

Mr. WOOD of Idaho. Mr. Chairman, will the gentleman yield?

Mr. HALE. I yield to the gentleman from Idaho.

Mr. WOOD of Idaho. Is it not a fact, sir, that habit-forming drugs are no part of this bill at all, that they are under the Harrison antinarcotic law?

Mr. HALE. I must confess to the gentleman I am not too familiar with the provisions of the Harrison antinarcotic law.

Mr. WOOD of Idaho. I believe that is the fact.

Mr. HALE. There are provisions of the Food and Drug Act of 1938 in reference to habit-forming drugs. I refer specifically to section 502 of the Food and Drug Act of 1938.

Mr. WOOD of Idaho. Nembutal and such drugs are spoken of as habit-forming drugs when as a matter of fact they are not habit-forming drugs.

Mr. HALE. That is precisely the situation which presents difficulties, because drugs which some people regard as dangerous and habit-forming are not so regarded by others.

Mr. Chairman, I am in favor of this bill in its present form. I would be more in favor of it with paragraph (B) on page 5 stricken out. Of course, if you strike out that paragraph, then it follows that you must strike out the paragraph relating to appeals on page 7 due to the fact that there is no necessity for appeals if you have no administrative discretion in the Federal Security Administrator. If you do have any kind of discretion in the Federal Security Administrator, you cannot draw your appeal provisions too carefully, and this appeal provision is very carefully drawn.

Mr. MASON. Mr. Chairman, will the gentleman yield?

Mr. HALE. I yield to the gentleman from Illinois.

Mr. MASON. Do I understand that the gentleman approves two provisions of the bill but disapproves of the other and that in spite of the fact there is one section of the bill the gentleman disapproves of he feels the over-all picture is such that it would be better to adopt the bill and swallow the part that he does not approve of?

Mr. HALE. The gentleman characterizes my position fairly accurately. I think that the present state of the law is so unsatisfactory to the druggist and the consumer that the Congress must legislate to clear it up. It should do so without delay.

Mr. HESELTON. Mr. Chairman, I ask unanimous consent to extend my remarks at this point in the RECORD.

The CHAIRMAN. Is there objection to the request of the gentleman from Massachusetts?

There was no objection.

Mr. HESELTON. Mr. Chairman, this legislation, as recommended by the Committee on Interstate and Foreign Commerce by a vote of 19 to 4, is a carefully considered proposal in a field which is admittedly difficult and technical.

Legislation was proposed in substantially the same form as H. R. 3298 in the second session of the Eighty-first Congress.

The committee held hearings on 5 days, two being full-day sessions. Its consideration of the legislation in executive session covered 7 days. The bill itself, as reported, is clear evidence of the efforts made by the committee to present to the House as sound and workable legislation as could be devised.

So far as I know, there is little, if any, objection to the provisions authorizing oral prescriptions or refills of prescriptions. Consequently, I would like to discuss briefly the provisions for establishing a list of drugs and the provision for judicial review.

Admittedly, the provision for establishing a list of drugs gives rise to the main controversy which exists as to this bill.

The National Association of Retail Druggists, representing some 35,000 retail drug-store owners throughout the Nation, supports this provision.

The American Pharmaceutical Association, which is described as a national, nonprofit, professional body of pharmacists, pharmaceutical educators, law-enforcement officials, research workers, and others interested in the protection of public health and the prevention and treatment of disease, is opposed to this provision. That is also true of the American Pharmaceutical Manufacturers Association, which has over 200 members in this country and in Canada; of the American Drug Manufacturers Association, which has 67 members, a list of which is included at page 150 of the hearings; and of the Proprietary Association, which consists of about 150 members.

However, I think it should be made clear that in connection with the opposition expressed by the American Pharmaceutical Association there is clearly a difference of opinion among its membership.

First, when Mr. Robert P. Fischelis, secretary and general manager of the association, was testifying before the committee I inquired if it was not a fact that the National Association of Retail Druggists included in its membership a great many pharmacists, and he replied that it did. It is, therefore, obvious that those pharmacists who support the position of the National Association of Retail Druggists are in disagreement with the American Pharmaceutical Association.

Next, I am sure that we all have had indications of differences of opinion among the pharmacists as to the position taken by their national association.

The gentleman from Washington [Mr. MITCHELL] brought that to our attention forcibly yesterday afternoon when he included in the RECORD the telegram which reported that the pharmacists of the State of Washington, in convention at Yakima, unanimously endorsed the bill, and when he included similar endorsements from the dean of the College of Pharmacy at the University of Washington and the professor of pharmaceutical chemistry at that university. These will be found at page 9236 of the RECORD.

Further evidence of this disagreement appears in the telegram at page 9240 of the RECORD from the secretary of the Illinois Pharmaceutical Association to the gentleman from Illinois [Mr. SABATH] urging that a rule be granted on this bill.

I assume that all of us have received telegrams from people who are sincerely in opposition to this provision, using almost identical language, to the effect that the one who sent the telegram "is vigorously opposed to subparagraph (B) of paragraph (1) of this bill" and describing it as containing "unnecessary and arbitrary powers proposed to be granted to the Federal Security Administrator."

I think there is no question but that the granting of any extensive power to the present Federal Security Administrator immediately gives rise to serious concern in the minds of a great many people. However, it seems clear to me that if we are to accomplish anything in a field which admittedly requires definite and affirmative action, we must recognize that some agency must be given the power to do such things as will eliminate, as far as humanly possible, the confusion and uncertainty which now prevails.

During the executive consideration of the bill I tested the possibility of providing for action by the professional and trained group charged with the day-to-day administration of the Food and Drug Act, but I must admit that I think any such proposal could not stand the test of considered action. Rather, I think we must accept the factual situation which exists and rely upon the probability that these professional and competent people will, in large measure, do the actual work involved and upon what I believe to be a completely satisfactory provision for judicial review. Beyond that, is the clear fact that should there be any instances of arbitrary, unwise or unsound administration, Congress can and undoubtedly would take prompt remedial action.

I think I should add that the hearings disclosed an attitude on the part of the Administrator which is certainly commendable. He repeatedly emphasized that while the situation could be partially dealt with through regulation and, in fact, furnished the committee with the text of a regulation which was under consideration, he felt the subject was of such importance and of such complexity that he believed it ought to be dealt with in a comprehensive way, by legislation rather than by administrative regulation.

There is another phase of this problem which has seemed to me to be of great importance. Under the situation prevailing now the druggists and pharmacists find themselves in a position where they are constantly confronted with the possibility of criminal prosecution or seizure in order to determine the legality of their action in selling certain drugs. It seems to me obviously preferable and in the clear interest of the druggists, the pharmacists, the physicians, and the public generally, that instead of a prolonged series of criminal prosecutions or seizures in order to distinguish between prescription drugs and over-the-counter drugs, the over-all recommendation of the committee should carry great weight with the membership of this House. In that connection I recommend reading three paragraphs of the committee report at pages 9 and 10 entitled "Proposed Statutory List," "Case-by-Case Judicial Determination," and "Considerations Which Influenced the Committee's Decision."

The provision for judicial review is a vitally important part of this legislation. Under the amended bill, the provisions of section 701 (e) and (g) of the present law will insure that any interested person may obtain judicial review by a United States court of appeals and, upon certiorari, by the Supreme Court of the United States.

As a result of the recent decision of the Supreme Court of the United States in the Universal Camera Corp. against NLRB, there is very definite guaranty now that the reviewing courts are not limited to a mere finding in the record of evidence which, when viewed in isolation, substantiated the administrative agency's finding but, rather, they are required to review the case upon the whole record in making a determination where the administrative ruling is supported by substantial evidence. The testimony of Hon. Harold M. Stephens, Chief Judge of the United States Court of Appeals for the District, is extremely important and I am certain was considered by every member of the committee as a most effective contribution to the consideration of this phase of the bill. All of his testimony will be of value to anyone who is concerned about the problem of arbitrary or capricious action by administrative agencies without the possibility of adequate review in our courts.

In conclusion, and in connection with this phase of the problem, I wish to quote four paragraphs from his testimony which I am convinced constitute a very important part of the legislative history of this bill and, in fact, provide a most thoughtful expression from one of our ablest jurists. The quotation follows:

> I wish to add, if I may, that I am in sympathy with the requirements of Congress in the Administrative Procedure Act, and I am sure that all judges in the district courts and circuit courts of appeal are fully in sympathy with the requirements of the Congress in the Administrative Procedure Act. Wherever we do review the action of the commissions we do so upon the whole record in determining whether the administrative ruling is supported by substantial evidence.
>
> While I had to obey the rule, because I am bound by the decisions of the Supreme Court as a circuit judge, I did not at all sympathize with—and I am sure I reflect the view of the whole circuit court of appeals when I say we did not at all sympathize with restricted powers of review accorded to us by the earlier decisions of the Supreme Court. But the Supreme Court has recanted and confessed its error in those respects in these two recent cases—the Universal Camera and the Pittsburgh cases. And the Congress has also corrected the rule governing our scope of review in the Administrative Procedure Act. • • •
>
> I would like to add just this, before I close: I can assure you that the circuit courts of appeal of this country, who are the courts of last resort in the Federal system except in the few cases that go to the Supreme Court, feel a very real responsibility in dealing with these commission appeals. We feel the same responsibility we do in reviewing the decisions of the United States district courts, to see to it that the litigants have had a fair hearing and that the Administrator's findings are supported by substantial evidence and are not arbitrary.
>
> I might remind you that in the Administrative Procedure Act passed by this Congress, in the review section it has been made necessary for the circuit courts of appeals to go as far as this. You have said to us: "So far as necessary to decision and where presented the reviewing court shall decide all relevant questions of law, interpret constitutional and statutory provisions, and determine the meaning or applicability of the terms of any agency action. It shall (A) compel agency action unlawfully withheld or unreasonably delayed; and (B) hold unlawful and set aside agency action, findings, and conclusions found to be (1) arbitrary, capricious, and abuse of discretion, or otherwise not in accordance with law; (2) contrary to constitutional right, power, privilege, or immunity; (3) in excess of statutory jurisdiction, authority, or limitations, or short of statutory right; (4) without observance of procedure required by law; (5) unsupported by substantial evidence." So we do have, imposed by you, a solemn responsibility, and I assure you we discharge it with deliberation and pains.

Mr. CROSSER. Mr. Chairman, I yield 5 minutes to the gentleman from Florida [Mr. ROGERS].

Mr. ROGERS of Florida. Mr. Chairman, I want to first preface my remarks by saying this bill is sponsored and introduced by the distinguished gentleman from North Carolina [Mr. DURHAM], one of the outstanding Members of this House, one who is a druggist and a pharmacist.

Mr. Chairman, it seems to me that we have gotten into a lot of discussion that is not pertinent to the provisions or purposes of this bill. I want to say this, that your committee studied this bill; they had executive sessions on this bill; this bill was discussed thoroughly; it came out of your committee with a vote of 19 to 4. There were four who were not in accord with the provisions of this bill.

In order that we might see what we are doing here, let us see what the present law is and just what we want to do. In the first place, under the present act there is confusion in the administration of this law even among the manufacturers, because some of them put out a drug that is to be dispensed only on the

prescription of a doctor, whereas on that same identical drug, if it is made by another manufacturer, it can be sold over the counter. Now, this confusion must be righted here.

Here is another thing. Under the present law you cannot have a prescription refilled unless the doctor, who gave that prescription, says it is refillable. Now, we have incidents like this. Here is a farmer or a merchant who goes to the doctor and he possibly wants to get aspirin—I am using that as an example—and he is given a prescription for aspirin. Unless the doctor says this is refillable—and of course, the farmer does not know what it is—he cannot go back there to the pharmacist or the druggist and have it refilled under the present law. Now this law that we are trying to establish here will permit those prescriptions to be refilled if the medicine is not dangerous, or if it is not toxic or it is not a habit-forming drug. Now that is one thing.

Another thing under the present law, you take doctors, you cannot always get to them; you cannot always get to the druggist, and they cannot telephone in to the druggist for the prescription. They cannot telephone the prescription to the druggist under the present law, and that should be corrected. This law corrects that; he is permitted to do that, with this proviso, that it be immediately written down, so the druggist has a record of what the prescription is, so in the event there is any harmful result coming from the prescription you can lay the blame where it belongs. That is another thing. Under the present law, that also is up to the Administrator. When a druggist or pharmacist sells some drug without a prescription, a drug that is dangerous or that is habit-forming, the Administrator has to go down there and prosecute that man. Under this law the druggist or the pharmacist will know before he sells it whether it is a prescription drug, or whether it is a drug that can be sold over the counter.

Those are the things we are trying to cure. Is there anything objectionable to that? The American Medical Association did not object to this bill. We had weeks of hearings on it, and they did not come in there and object to any provision of this bill.

This seems to me to be a bill with some virtue attached to it, with some merit to it. It is a bill that is endorsed by the druggists and the pharmacists. This is a bill which will bring some remedy into the present situation which we find ourselves in, and I hope that this House will adopt it.

Mr. WILLIAMS of Mississippi. Mr. Chairman, I yield myself 2 minutes.

Mr. Chairman, this bill is much needed legislation. What the American druggist is seeking is certainty in dispensing drugs. The bill as written will give him certainty. If the language in subsection (b) (1) is eliminated and the O'Hara language is substituted therefor, all of the certainty that is given to the druggist in this bill will be removed, and the druggist will find himself in the same predicament in which he finds himself under the present law.

Mr. KLEIN. Mr. Chairman, will the gentleman yield?

Mr. WILLIAMS of Mississippi. I yield to the gentleman from New York.

Mr. KLEIN. Just to clear up an uncertainty here, and I know it has been stated by the gentleman and by many Members on the floor, is it not a fact that this legislation if enacted would benefit the small-business man, the small druggist, throughout the country?

Mr. WILLIAMS of Mississippi. Not only would it benefit the small druggist but it would also afford protection to the public against the dangers of buying toxic drugs over the counter.

Mr. KLEIN. Does not a relative of the gentleman, I believe his father, run a small drug store?

Mr. WILLIAMS of Mississippi. Yes; but I am not taking part in this debate on the basis of setting myself up as an expert by any means; I am not a druggist.

Mr. MEADER. Mr. Chairman, will the gentleman yield?

Mr. WILLIAMS of Mississippi. I yield to the gentleman from Michigan.

Mr. MEADER. If the language could be so drafted as to protect the druggist without giving dictatorial power to the Federal Security Administrator, would the gentleman object to such an amendment?

Mr. WILLIAMS of Mississippi. That is what the bill does. I am supporting the language that is in the bill, because it does the very same thing the gentleman seeks to do, that is, to delegate this authority to the Administrator and then tie his hands so that he cannot abuse that authority.

The CHAIRMAN. All time has expired.

The Clerk will read the bill for amendment.

Mr. HARRIS. Mr. Chairman, a parliamentary inquiry.

The CHAIRMAN. The gentleman will state it.

Mr. HARRIS. Mr. Chairman, is it not a fact that the substitute bill will be read in its entirety before amendments will be in order?

The CHAIRMAN. The gentleman is correct.

The Clerk read as follows:

Be it enacted, etc., That subsection (b) of section 503 of the Federal Food, Drug, and Cosmetic Act, as amended, is amended to read as follows:

"(b) A drug dispensed by filling or refilling a written or oral prescription of a practitioner licensed by law to administer such drug shall be exempt from the requirements of section 502, except paragraphs (a), (1) (2) and (3), (k), and (l), and the packaging requirements of paragraphs (g) and (h), if the drug bears a label containing the name and address of the dispenser, the serial number and date of the prescription, or of its filling, the name of the prescriber, and, if stated in the prescription, the name of the patient, and the directions for use and cautionary statements, if any, contained in such prescription. This exemption shall not apply to any drug dispensed in the course of the conduct of a business of dispensing drugs pursuant to diagnosis by mail or otherwise without examination of the patient. If the drug is intended for use by man and—

"(1) is a habit-forming drug subject to the regulations prescribed under section 502 (d);

"(2) has been found by the Administrator, after investigation and opportunity for public hearing, to be unsafe or ineffective for use without the professional diagnosis or supervision of a practitioner licensed by law;

"(3) if an effective application under section 505 limits it to use under the professional supervision of a practitioner licensed by law, such exemption shall apply only if such drug is dispensed upon a written prescription of a practitioner licensed by law to administer such drug or upon an oral prescription of such practitioner which is reduced to writing and filed by the pharmacist; or is dispensed by refilling a prescription if such refilling is authorized by the prescriber in the original prescription or by oral order and such order is reduced to writing and filed by the pharmacist.

"The Administrator may by regulation remove drugs subject to section 502 (d) and section 505 from the provision of this subsection when such requirements are not necessary for the protection of the public health.

"A drug which is subject to clause (1), (2), or (3) of this subsection shall be deemed to be misbranded if at any time prior to dispensing its label fails to bear the statement 'Caution: Federal law prohibits sale or dispensing without prescription.'

"The act of dispensing a drug contrary to the provisions of this subsection shall be deemed to be an act which results in the drug's being misbranded while held for sale.

"Any interested person may file with the Administrator a petition proposing the addition to, or deletion from, the list of drugs promulgated by the Administrator in accordance with clause (2) hereof. Such petition shall set forth the proposal in general terms and shall state reasonable grounds therefor. The Administrator shall give public notice of the proposal and an opportunity for all interested persons to present their views thereon, orally or in writing, and as soon as practicable thereafter shall make public his action upon such proposal. At any time prior to the thirtieth day after such action is made public any interested person may file objections to such action, specifying with particularity the changes desired, stating reasonable grounds therefor and requesting a public hearing upon such objections. The Administrator shall thereupon, after due notice, hold such public hearing. As soon as practicable after completion of the hearing, the Administrator shall by order make public his action on such objections.

"An order so issued by the Administrator may, within 90 days after its issuance, be appealed by any interested person in accordance with the provisions prescribed in section 701 (f) and (g) of this Act, except that an appeal from the Administrator's order issued hereunder shall be in the nature of a trial de novo, without presumptions in favor of either party to such appeal.

"The provisions of this section of the act shall not be applicable to drugs now included or which may hereafter be included within the classifications stated in section 2220 of the Internal Revenue Code (26 U. S. C. 2220), or to marijuana as defined in section 2228 (b) of the Internal Revenue Code (26 U. S. C. 288 (b))."

With the following committee amendment:

Strike out all after the enacting clause and insert the following: "That subsection (b) of section 503 of the Federal Food, Drug,

and Cosmetic Act, as amended, is amended to read as follows:

"'(b) (1) A drug intended for use by man which—

"'(A) is a habit-forming drug to which section 502 (d) applies; or

"'(B) because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, has been determined by the Administrator, on the basis of opinions generally held among experts qualified by scientific training and experience to evaluate the safety and efficacy of such drug (and, where a public hearing is required by paragraph (5), on the basis of evidence adduced at such hearing by such experts), to be safe and efficacious for use only after professional diagnosis by, or under the supervision of, a practitioner licensed by law to administer such drug; or

"'(C) is limited by an effective application under section 505 to use under the professional supervision of a practitioner licensed by law to administer such drug,

shall be dispensed only (i) upon a written prescription of a practitioner licensed by law to administer such drug, or (ii) upon an oral prescription of such practitioner which is reduced promptly to writing and filed by the pharmacist, or (iii) by refilling any such written or oral prescription if such refilling is authorized by the prescriber either in the original prescription or by oral order which is reduced promptly to writing and filed by the pharmacist. The act of dispensing a drug contrary to the provisions of this paragraph shall be deemed to be an act which results in the drug being misbranded while held for sale.

"'(2) Any drug dispensed by filling or refilling a written or oral prescription of a practitioner licensed by law to administer such drug shall be exempt from the requirements of section 502, except paragraphs (a), (1), (2), and (3), (k), and (l), and the packaging requirements of paragraphs (g), and (h), if the drug bears a label containing the name and address of the dispenser, the serial number and date of the prescription or of its filling, the name of the prescriber, and, if stated in the prescription, the name of the patient, and the directions for use and cautionary statements, if any, contained in such prescription. This exemption shall not apply to any drug dispensed in the course of the conduct of a business of dispensing drugs pursuant to diagnosis by mail or otherwise without examination of the patient or to a drug dispensed in violation of paragraph (1) of this subsection.

"'(3) The Administrator may by regulation remove drugs subject to section 502 (d) and section 505 from the requirements of paragraph (1) of this subsection when such requirements are not necessary for the protection of the public health.

"'(4) A drug which is subject to paragraph (1) of this subsection shall be deemed to be misbranded if at any time prior to dispensing its label fails to bear the statement "Caution: Federal law prohibits dispensing without prescription." A drug to which paragraph (1) of this subsection does not apply shall be deemed to be misbranded if at any time prior to dispensing its label bears the caution statement quoted in the preceding sentence or any other statement which represents or implies that the dispensing of the drug without the prescription of a licensed practitioner is prohibited.

"'(5) Any interested person may file with the Administrator a petition proposing the making of a determination, or the modification of a determination made or proposed to be made, by the Administrator pursuant to subparagraph (B) of paragraph (1). The filing of a petition for the purpose of opposing a proposed determination that a drug is one to which such subparagraph (B) applies shall stay the operation of paragraph (1) with respect to such drug until a petition for judicial review can be filed and interim relief sought under section 10 (d) of the Administrative Procedure Act. The petition shall set forth in general terms the proposal contained therein, and shall state reasonable grounds therefor. The Administrator shall give public notice of the proposal made in the petition and shall give to all interested persons a reasonable opportunity to present their views thereon, orally or in writing, and as soon as practicable thereafter shall make public his action on the proposal. At any time prior to the thirtieth day after such action is made public, any interested person may file with the Administrator objections to such action, specifying with particularity the changes proposed, stating reasonable grounds therefor, and requesting a public hearing for the taking of evidence of experts who are qualified by scientific training and experience to testify on the question of whether the drug in question is safe and efficacious for use only after professional diagnosis by, or under the supervision of, a practitioner licensed by law to administer such drug. The Administrator shall thereupon, after appropriate notice, hold such public hearing. As soon as practicable after the hearing, the Administrator shall make his determination and issue an appropriate order. The Administrator shall make his order only after a review of the whole record and in accordance with the reliable, probative, and substantial evidence, and shall make detailed findings of the facts on which he based his order. Such order shall be subject to judicial review in accordance with the provisions of section 701 (f) and (g).

"'(6) Nothing in this subsection shall be construed to relieve any person from any requirement prescribed by or under authority of law with respect to drugs now included or which may hereafter be included within the classifications stated in section 3220 of the Internal Revenue Code (26 U. S. C. 3220), or to marihuana as defined in section 3238 (b) of the Internal Revenue Code (26 U. S. C. 3238 (b)).'

"SEC. 2. The provisions of this act shall take effect 6 months after the date of its enactment."

Mr. ROBERTS. Mr. Chairman, I offer an amendment.

The Clerk read as follows:

Page 6, line 11, strike out "and efficacy"; and on page 6, lines 14 and 15, and page 8, lines 13 and 14, strike out "and efficacious for use only after professional diagnosis by, or under the supervision of," and insert "for use only under the supervision of."

Mr. ROBERTS. Mr. Chairman, when this bill was being considered in committee there was quite a difference of opinion as to the meaning of the word "efficacy" and the meaning of the word "efficacious." Webster's dictionary defines efficacious to mean possessing the quality of being effective. Many of us feel perhaps that is too broad and in fact many of us voted to strike those words out in committee. I feel the bill will be just as good and will accomplish the same purpose and will answer some of the objections being made along the line that we are giving too much power to the Administrator.

Mr. WILLIAMS of Mississippi. Mr. Chairman, will the gentleman yield?

Mr. ROBERTS. I yield.

Mr. WILLIAMS of Mississippi. I am in accord with the gentleman's amendment as I think practically every other member of the committee now is. Of course I cannot speak for the committee but the committee took action on this language and voted to leave the language in the bill. However, subsequent developments, I believe, have shown that language is superfluous and should be taken out. There has been a great deal of dispute over the words "efficacy" and "efficacious." The objections to those words are based on fears that the Federal Security Administrator would have the power to ban drugs from the market entirely if he decided that they are not efficacious. The majority report pointed out that such was not the intention of the bill and that the objections arise because of the failure to read the entire language of the paragraph. The purpose was to require that drugs which are not poisonous but which are nevertheless unsuitable for use by laymen must be dispensed on prescription only. I hope this amendment will not meet with any opposition. I feel that this amendment eliminates the dangers which are anticipated in this bill by the gentleman from Minnesota, that is, the granting to the Federal Security Administrator of improper or unwarranted authority.

Mr. HESELTON. Mr. Chairman, will the gentleman yield?

Mr. ROBERTS. I yield.

Mr. HESELTON. I think it might be helpful to anyone who is doubtful about the wisdom of this amendment if I call attention to the fact that when this mater was discussed with Mr. Ewing he finally said as to these words, "We think this adds something to the protection of the bill, but it is nothing I would die for." In other words, they themselves admit there is a question as to the desirability of having these words in the bill. Personally it seems to me that we should go ahead with the provisions with regard to safety and that we might well postpone action on this doubtful use of these words which the gentleman seeks to strike out.

Mr. ROBERTS. I thank the gentleman for his remarks.

The CHAIRMAN. The time of the gentleman has expired.

Mr. O'HARA. Mr. Chairman, I rise in opposition to the amendment.

Mr. Chairman, this bill was originally sold to you as the perfect bill. What has just happened illustrates that my distinguished committee has now changed its mind or at least a part of the membership of it has changed its mind on the question of amendments that it is desirable to have in the bill.

Mr. WILLIAMS of Mississippi. Mr. Chairman, will the gentleman yield?

Mr. O'HARA. I yield.

Mr. WILLIAMS of Mississippi. The gentleman knows I supported the amendment to take the word "efficacious" out of the bill in committee.

Mr. O'HARA. That is one of the objections I have to the bill. But I have an amendment which I think will do a much better job than the amendment offered by the gentleman.

Mr. WILLIAMS of Mississippi. The gentleman agrees that the position we have taken is that this language should be stricken out of the subsection in which it presently appears in the bill; does he not?

Mr. O'HARA. I think it is a fair comment to say it illustrates that one of the

members of the committee is now unhappy about the language and that the gentleman from Mississippi [Mr. WILLIAMS] who has been most active in charge of this bill is unhappy about some of this language. I am unhappy about some more of it and as soon as this amendment is disposed of I hope to offer an amendment which will get at the meat of this thing.

Mr. BENNETT of Michigan. Mr. Chairman, will the gentleman yield?

Mr. O'HARA. I yield.

Mr. BENNETT of Michigan. The reason they are unhappy about it is the very point we have tried to make—because it gives too much authority to the Federal Security Administrator. I think the gentleman from Mississippi [Mr. WILLIAMS] will admit that.

Mr. O'HARA. He so stated, as I understood him.

Mr. HESELTON. Mr. Chairman, will the gentleman yield?

Mr. O'HARA. I yield to the gentleman from Massachusetts.

Mr. HESELTON. I am sure the gentleman would agree that it is only fair to the members of the committee which considered this bill to state that I submitted a motion to strike those words from the bill, and that there was a very close vote. So that it was pinpointed to these very words.

Mr. O'HARA. The gentleman is correct.

Mr. PRIEST. Mr. Chairman, will the gentleman yield?

Mr. O'HARA. I yield to the distinguished gentleman from Tennessee.

Mr. PRIEST. I just want to state, along with the gentleman from Massachusetts [Mr. HESELTON], that I supported the amendment in the committee to strike the words, and I think they should go out.

Mr. O'HARA. Let me say to the gentleman from Tennessee [Mr. PRIEST] that I think he is a little bit troubled about section 5 also. I hope he will give me the same support on my amendment. I intend to offer the amendment which I indicated in my previous remarks. I am not speaking for the gentleman's conscience, because I know he is very honest about it.

Mr. WOLVERTON. Mr. Chairman, will the gentleman yield?

Mr. O'HARA. I yield to the gentleman from New Jersey.

Mr. WOLVERTON. The thought has been expressed several times that some members of the committee were unhappy, after further consideration, about having the words now under consideration in the bill. I do not think it is a question of happiness or unhappiness that suggests this amendment. I think the amendment is suggested to make those who are opposed to the words a little happier by striking the words out of the bill.

Mr. O'HARA. I have in mind that some of the 19 Members who strongly supported the bill are now anxious to amend it.

I trust the amendment will be voted down, so that we can get to my amendment correcting the entire subsection (b) and this obnoxious subsection (5). I will say that striking out the word "efficacy" makes it a little more palatable, but not palatable enough.

Mr. CRAWFORD. Mr. Chairman, will the gentleman yield?

Mr. O'HARA. I yield to the gentleman from Michigan.

Mr. CRAWFORD. To what group of people does the language on line 10, page 5, refer, where it says: "Experts qualified by scientific training and experience"?

Mr. O'HARA. I will tell you what that means. That means that you are giving to the Administrator the right to call in anybody; and he determines who is the expert, does he not?

Mr. CRAWFORD. That is my understanding.

Mr. O'HARA. Of course. He is going to take his opinion, and when he makes that decision you will never get a reversal in any circuit court or Supreme Court in the United States.

Mr. CRAWFORD. May I ask one other question?

Assuming that a man with great experience and scientific training did attempt to say that a drug was efficacious: On what ground can he do that? What scientific knowledge gives him the ability to say that a certain drug will cure my cold when my cold might be caused by something he knows nothing about?

Mr. O'HARA. The gentleman has opened the way to a realm of speculation that is as vast as the heavens. A drug which might be efficacious to the gentleman might be deadly to me.

Mr. CRAWFORD. Certainly. Anybody who has dealt with drugs or who has bought patent medicines, hydrocol, or otherwise, without diagnosing the case, these scientific men cannot tell. We have thousands of them under the soil now who were put there by men who did not know what they were doing.

The CHAIRMAN. The time of the gentleman from Minnesota [Mr. O'HARA] has expired.

Mr. HARRIS. Mr. Chairman, I move to strike out the last word.

Mr. Chairman, it is quite obvious that because of the technicality of this legislation there is a great deal of confusion. I can readily understand that. This committee wrestled with this problem for many, many weeks. The very word in question here, "efficacy" or "efficacious," was a matter of discussion over a long period of time.

I respect the views of the gentleman from Minnesota [Mr. O'HARA] and those who are opposed to the provisions of this bill affecting the determination of what drugs will be safe and dispensed over the counter or by prescription. When this motion to strike out this word was offered in committee, I voted against it. There is some question as to the effect of it. It is a highly technical provision. I will say to my colleagues that in my opinion you do not understand just the meaning of it. Take the word as presented to us here as it applies to the Food and Drug Act, it has a lot of meaning in the legislation. In my opinion because of the history behind it and as in the regulation administered by the Food and Drug people it adds something to the Food and Drug Act. I am not going to oppose striking it out, because after further consultation with so many who feel that it would have a different application, I think perhaps time will prove to us that it may be necessary to change the definition in the Food and Drug Act of the word "safe" and the Congress is going to have to do it.

Under the definition of the Food and Drug Act of the word "safe" it applies to poisonous drugs, those drugs that are toxic; and anyone knows—and I am not an expert in the drug business—anyone knows there are many drugs on the market that are not poisonous, that are not toxic, but yet they would have an ill effect upon a human being.

I may also say that if this word is stricken out, which it probably will be, it may very well be necessary that we come back in here at a later time and redefine the word "safe" in the interest and the protection of the public.

There has been a lot of confusion about just what this means, the whole act itself; and I think the debate has been very helpful. Certainly they are questions for argument. But when the question is finally resolved this issue means: Are you going to adopt legislation that will provide someone with the authority to determine after obtaining information from the experts in the field what is best for the general public? Or are you going to leave it to the commercial interests? That is the whole issue that we have before us here to determine. Certainly I am not for giving some administrator or bureau wide latitude and authority to impose himself upon any commercial interest or the people——

Mr. SMITH of Wisconsin. Mr. Chairman, will the gentleman yield?

Mr. HARRIS. I am interested in just what the gentleman is interested in, the protection of the people of this country.

I yield to the gentleman from Wisconsin.

Mr. SMITH of Wisconsin. Why is not that a matter for the States to determine?

Mr. HARRIS. The States cannot possibly determine that because manufacturers of drugs ship in interstate commerce, and the States could not possibly control it.

Mr. SMITH of Wisconsin. We have State control now to a considerable degree.

Mr. HARRIS. This does not affect that.

Mr. HESELTON. Mr. Chairman, I move to strike out the last word.

Mr. Chairman, I think it is only fair and may be helpful to the Members who are seriously concerned about the situation which does in fact affect the druggists and pharmacists of this country as well as the general consuming public, if further attention is given to the charge that it might be possible for Mr. Oscar Ewing somehow or other, under the terms of this bill, arbitrarily to make a determination based upon testimony or opinions of a loaded set of experts as to the listing of a drug.

I know, and I want to stress this again, that this bill came out of committee by a vote of 19 to 4. I have the highest regard for my four colleagues on my own side of the House who differ

with the majority of the members of the committee. They have had a full opportunity this afternoon to explain their position. I think it may only be fair for some of the rest of us who worked on this bill to try to clear up some of the existing confusion.

What we are talking about is found in this language on page 5:

Because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, has been determined by the Administrator—

Certainly he has to make a determination. Somebody has to. I do not believe there is any other way by which we can provide for its determination except through some official in the executive department; we gave some consideration to a legislative list but decided that was impossible.

Then the bill continues—

on the basis of opinions—

Not the opinions of the department's executives but of opinions—

generally held among experts qualified by scientific training and experience to evaluate the safety and efficacy of such drug.

What does that mean? Every reputable drug manufacturer in this country has a staff of recognized experts. You know and I know that all of the colleges of pharmacy have a staff of recognized experts. There are textbooks, many of them recognized as authoritative. Now, all that is what the committee intended should be taken into account when these determinations are made.

Then further:

Where a public hearing is required by paragraph (5), on the basis of evidence adduced at such hearing by such experts.

What experts? Not only the experts of the department but experts from private life, from private industry, from educational institutions, experts who have an established reputation in the field.

Going one step further, I wish there was time for you to examine all of the testimony. There is provision for judicial review, which my colleague from Minnesota admits is tied up with this. In a case decided in the United States Supreme Court in February of this year there has been a sharp change in review procedure. There is now an absolute and a definite requirement that the reviewing court shall take into consideration the entire record, not what we had to contend with before, where it could simply find that the administrative agency's ruling was correct if there was any evidence in support of it. If you will read the testimony of Chief Justice Stephens of the circuit court of appeals I think you will be impressed with the fact this committee has sought to surround action by this particular agency with every kind of a safeguard it could think of.

I suggest that all this talk, all of this fear that has been expressed this afternoon because Oscar Ewing happens to be the present individual who would have to put his name to some sort of determination is something that is unwarranted. We know that all of the druggists are begging for action on this. Yesterday we had telegrams presented to us from pharmacists in the State of Washington and another from the State of Illinois in reference to the matter urging enactment of the committee bill. I know the members of the committee realize that there are many pharmacists who feel this is absolutely necessary. We have no authentic information that any physicians are opposed to it.

I think the major problem that confronts us is that we have a situation that is confusing and uncertain, which can only be determined by a series of criminal prosecutions or seizures or injunctions and harassment of the druggists and pharmacists of the country. I suggest that the basic reason for our support of this legislation should be in the interest of public health and the general welfare of the people who must depend on us to provide sane and constructive legislation.

Mr. BECKWORTH. Mr. Chairman, will the gentleman yield?

Mr. HESELTON. I yield to the gentleman from Texas.

Mr. BECKWORTH. One of the important reasons why the druggists throughout the country want this legislation may be found on page 96 of the hearings. There is a list of well over 100 or 150 who have been convicted for the over-the-counter sale of drugs, many of these people, I dare say, selling them innocently. They do not like it and they want it changed.

The CHAIRMAN. The time of the gentleman from Massachusetts has expired.

Mr. KERSTEN of Wisconsin. Mr. Chairman, I ask unanimous consent that the gentleman may proceed for two additional minutes.

The CHAIRMAN. Is there objection to the request of the gentleman from Wisconsin?

There was no objection.

Mr. KERSTEN of Wisconsin. Mr. Chairman, will the gentleman yield?

Mr. HESELTON. I yield to the gentleman from Wisconsin.

Mr. KERSTEN of Wisconsin. I would like to ask the gentleman a question with reference to his argument relating to the phrase "opinions generally held among experts." May I ask the gentleman who makes the determination as to what these opinions are? Is it not the Administrator?

Mr. HESELTON. The Administrator, of course, subject to review of the court on a much broader scale than had been in existence prior to February of this year.

Mr. BENNETT of Michigan. Mr. Chairman, will the gentleman yield?

Mr. HESELTON. I yield to the gentleman from Michigan.

Mr. BENNETT of Michigan. What is there to review if the Federal Security Administrator has three experts and the drug industry has three experts?

Mr. HESELTON. I have already indicated the nature of the expert testimony and opinions. Then the courts have to review the full record, as the gentleman well knows, and they now have to make a decision taking into consideration the full record.

The CHAIRMAN. The time of the gentleman from Massachusetts has again expired.

Mr. WILLIAMS of Mississippi. Mr. Chairman, I move to strike out the last word.

Mr. Chairman, in regard to the question the gentleman asked, here is the scope of a review under the Administrative Procedures Act:

(e) So far as necessary to decision and where presented the reviewing court shall decide all relevant questions of law, interpret constitutional and statutory provisions, and determine the meaning or applicability of the terms of any agency action. It shall (A) compel agency action unlawfully withheld or unreasonably delayed; and (B) hold unlawful and set aside agency action, findings, and conclusions found to be (1) arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law; (2) contrary to constitutional right, power, privilege, or immunity; (3) in excess of statutory jurisdiction, authority, or limitation, or short of statutory right; (4) without observance of procedure required by law; (5) unsupported by substantial evidence in any case subject to the requirements of sections 1008 and 1007 of this title or otherwise reviewed on the record of an agency hearing provided by statute; or (6) unwarranted by the facts to the extent that the facts are subject to trial de novo by the reviewing court. In making the foregoing determinations the court shall review the whole record or such portions thereof as may be cited by any party, and due account shall be taken of the rule of prejudicial error.

I hope that answers the gentleman's question.

In support of the amendment offered by the gentleman from Alabama, I would like to ask the gentleman from Minnesota a question: Is it not a fact that he purposely left the words "efficacious" and "efficacy" out of the amendment which he will offer a little later on?

Mr. O'HARA. I suppose when we come to that and dispose of this it is not important. Of course, I am leaving it out. I am rewriting the whole section. As long as the gentleman is talking about this review business, does he know that one of the food and drug provisions on appeals provides as follows: "The findings of the Administrator as to the facts, if supported by substantial evidence, shall be conclusive," which means that there is practically no review at all?

Mr. WILLIAMS of Mississippi. The gentleman knows that the court has a right to determine whether the Administrator's decision is based on substantial evidence, and if it is based on substantial evidence the decision cannot be questioned.

Mr. Chairman, I ask for a vote on the amendment and hope that it will be adopted.

Mr. MILLER of Nebraska. Mr. Chairman, I move to strike out the last two words.

Mr. Chairman, I can see that this is a rather complicated bill. I might say that the committee appointed by the House, the Special Committee on Foods, Fertilizers, and Chemicals, has been holding some hearings over a period of more than a year now and has been wrestling with some of the problems we

have in this bill. For instance, in the bread hearings, as to whether or not softeners in breads and certain chemicals were harmful. We came to this determination, while we have not presented any legislation, we thought instead of leaving it up to an administrator to make a decision of vast importance, that would have such wide effect on industry and upon the public, that perhaps a board should be set up, a board of experts, who would make the decision for the administrator. In any law or any legislation you pass, there must be someone who is going to make decisions.

Coming back to our hearings on the use of chemicals, pesticides, and fertilizers, do you know that there are nearly 800 chemicals knocking at the door of the food industry for admission? Some 600 of them have been investigated. There are nearly 300 chemicals that we do not know what reaction they will have when they get into the blood stream. There is a tremendously wide field developing at a pace which is astonishing as to what chemical should be permitted, for instance in food. The Food and Drug Administrator or someone must be in position to make some of these decisions. It occurs to me that the bill now being considered gives too much power to the Administrator, I care not if he be a Democrat or a Republican. A commission, in my opinion, would be the better approach.

I am also concerned about the advertising in the newspapers and over television and the radio. It is a disgrace and an insult to human intelligence and jeopardizes the reputation of everyone who deals in the welfare of the sick. It is amazing how advertisers are permitted to hoodwink the public into buying worthless vitamins and other near useless products. The public needs protection from swindling quacks and medicine men. Many of the over-the-counter drugs and patent medicines are harmful.

Some of us may look a little askance at some of the fertilizers that come into the food stream, as to what happens to the children of this country, and what happens to some of these poisonous things that are being injected into the food stream. I am convinced that the Food and Drug Administration does not have enough power to determine those things quickly at this time.

Mr. HINSHAW. Mr. Chairman, will the gentleman yield?

Mr. MILLER of Nebraska. I yield to the gentleman from California.

Mr. HINSHAW. The gentleman suggests a board and that was considered at one time. I wonder if the gentleman will not agree that the decision of the Board that he proposes would be in effect identical with the advice the Administrator would receive under the terms of this bill.

Mr. MILLER of Nebraska. It should not be.

Mr. HINSHAW. Who would appoint the board?

Mr. MILLER of Nebraska. We would hope on that board that we planned in the legislation we hope to bring in industry, for instance. Industry may not always agree with the Administrator. We will have on the Board men of known chemical and research ability. We have had those experts before our committee. We would have somebody on there representing the Government and somebody representing the people. I think with that type of Board they could sit down and come to a conclusion which I think would be in the interest of the public.

Now, as to the different drugs, as a physician, I recognize that you have to have a good deal of leeway in permitting prescriptions to be filled. We speak about filling prescriptions by phone. It is not supposed to be done, according to the law, and some men have been caught by it. I think that half the prescriptions that are being filled today are filled this way. The doctor picks up the telephone and calls the druggist and says, "I want so-and-so filled." This is being done and you might as well make it legal, if it is against the law now, because they will continue doing it.

I also feel that the laws related to the issuance of barbiturates and the self-medication that presently is permitted ought to be tightened up.

I support the O'Hara amendment and trust the committee will give attention to a commission and not give so much power to an Administrator.

Mr. BONNER. Mr. Chairman, I move to strike out the last two words.

Mr. Chairman, I asked certain questions about this bill yesterday and received some answers, yet I am in doubt as to whether or not the language in this bill would not make it possible for those who manufacture and have been selling old-line prescriptions under patents to find themselves entangled in some rules and regulations that would be promulgated by the Administrator under this bill. This bill in itself gives the Administrator that power.

Mr. Chairman, I received the following telegram from the North Carolina Medical Society. I think in the State of North Carolina we have about as fine a group of practicing physicians and as fine a hospital system as will be found in any State in the Union.

The telegram is dated July 27, Raleigh, N. C., and is as follows:

RALEIGH, N. C., *July 27, 1951.*

Hon. HERBERT BONNER,
House of Representatives,
Washington, D. C.:

Reference bill 3298, Medical Society, State of North Carolina opposes those sections extending unwarranted authority granted Federal Security Administrator to codify drugs as to efficiency or to determine whether sold to public without prescription. These matters should be reserved to physicians, pharmacists authorized by State law to so function.

JAMES T. BARNES,
Executive Secretary, Medical Society of North Carolina.

When the medical society of my State comes out as strongly as this in opposition to a piece of legislation, which I admit I am unable to digest and to determine just what it contains, then I myself would think a long time and would want a great deal of explaining before I would support it.

Mr. Chairman, I think this bill covers more territory than has been discussed on the floor so far.

Mr. JENKINS. Mr. Chairman, will the gentleman yield?

Mr. BONNER. I yield to the gentleman from Ohio.

Mr. JENKINS. I have a telegram from the State medical society of the great State of Ohio to the same effect and import as the gentleman has received.

Mr. BONNER. In addition to that, I have received a telegram from an old established firm in North Carolina, the Vicks Chemical Co. In their organization they have chemists and pharmacists. They certainly have attorneys to advise them, and their attorneys have advised them, so I am told, that they might be called up before the Administrator and during the determination, by the Administrator of their product their product might be held from the market.

I have simply pointed to one instance, and there are others. So this might be an opening wedge to a piece of legislation which this House refused to adopt some time ago. I have great faith in the intelligence of men to prescribe sometimes for themselves; but when, as has been said here, one doctor might give me a prescription which might work for me and another doctor might give you a prescription which might work for you, and when some patent medicines do not cause the patient to respond as rapidly as other patent medicines do, I have my doubts as to the ability of one individual to determine all of these things. I do not know what the ability of the Administrator is to make all these determinations.

Mr. FENTON. Mr. Chairman, will the gentleman yield?

Mr. BONNER. I yield to the gentleman from Pennsylvania.

Mr. FENTON. The State of Pennsylvania Medical Society, with the endorsement of the American Medical Association, has no objection to authorizing the refilling of prescriptions, but they do object to section B.

Mr. BONNER. I thank the gentleman.

Mr. Chairman, I have not been able to discuss the bill with the author. He is a fine, grand gentleman. I know there are certain provisions in the bill which should be written into law to protect druggists and doctors, but beyond that I do not like to go. I would like to vote in support of a bill which would take the proper action to protect druggists and doctors, but I do not like this other part of the bill which has to do with determining the efficiency of medicines.

The CHAIRMAN. The time of the gentleman from North Carolina has expired.

Mr. HARRIS. Mr. Chairman, I ask unanimous consent that debate on this amendment close in 10 minutes.

The CHAIRMAN. Is there objection to the request of the gentleman from Arkansas?

There was no objection.

Mr. HOFFMAN of Michigan. Mr. Chairman, I move to strike out the last word.

Mr. Chairman, the gentleman from North Carolina [Mr. BONNER] seems to be laboring under the same doubts that I have in my mind. I can best illustrate

the arbitrary conduct of some of the Department's agents by citing a case of several years ago, when a manufacturing chemist, doing business in practically all of the United States, had quite a quantity of his products seized in several States because it was charged that they were mislabeled. I went to the Department and asked them to point out to me what was wrong about the labels and to give me some idea as to what should be printed on them so that our manufacturing chemists could properly label their products and comply with the law and the Department's regulations. There was no claim that the product was injurious. The complaint and seizure was on the ground that it was not technically properly labeled.

Do you know what the Department said? The Department said: "Oh, that is up to the manufacturer. Let them figure it out, and if it doesn't suit us we will seize their product."

I went one step further, and I said, "How about seizing it in the factory where it is put up and labeled?" "Oh, no," they said, "just wait until they ship it into other States, Indiana, Ohio, and so on, and then we will seize it."

The company suggested that the Department's agents come into the plant, go through every department and take from the shelves all products that they thought were either mislabeled or that contained ingredients which made the sale in interstate commerce unlawful. The company offered to waive, in writing, the question of whether the goods were in interstate commerce.

The Department's agents refused to do that. Then the company offered to ship the products into Indiana—the State line being only some 70 miles away—the Department could there seize merchandise which it claimed was misbranded or improperly manufactured.

The Department's agents refused to do that, but stated that they would and they did seize some of the company's products which they found on the shelves of purchasers who were located far from the point of manufacture.

Now you know that that arbitrary, unreasonable action served no good purpose. It seriously interfered with the company's business. For what small, or even large, retailer wants to have the local people know that merchandise sold by him has been seized because it was alleged by the Pure Food and Drug Department of Uncle Sam—that it was being sold in violation of law, was either a misbranded, injurious, or dangerous product.

Now, it is that sort of conduct that our people are afraid of, that I fear, this arbitrary, unreasonable attitude on the part of the administrators. That is one of the objections to this bill. Everyone wants to protect the health of our people, to prevent their being imposed upon by being sold products that are not properly labeled, but we do not like to have people on the Government payroll come along and make trouble just because they happen to have a little authority.

Mr. WILLIAMS of Mississippi. Mr. Chairman, will the gentleman yield?

Mr. HOFFMAN of Michigan. Yes, I yield to the gentleman.

Mr. WILLIAMS of Mississippi. I think the gentleman misunderstands what we are intending to do. That is really the thing we are seeking to remedy.

Mr. HOFFMAN of Michigan. I do understand what you are trying to do, but I know what the departments are trying to do. I know they can protect the people without a grant of additional power.

This department or agency is just like every other Federal, executive department—give anyone of them a little power over the activities of our people and immediately they seek more power, then more money to pay more employees. It is a strange but nevertheless characteristic trait of practically every agency or department of Government, whether it be Federal, State or local, to want more power, more employees, more funds—an opportunity to grow greater. A grant of arbitrary or even discretionary power always, unfortunately, seems to call for greater authority.

Let me give you another illustration, more recent, of arbitrary action by the department:

Section 204, subdivision (a) of the Federal Food, Drug, and Cosmetic Act as amended (21 U. S. C., sec. 342) defines adulterated food. It states:

A food shall be deemed to be adulterated: (a) (1) if it bears or contains any poisonous or deleterious substance which may render it injurious to health; but in case the substance is not an added substance such food shall not be considered adulterated under this clause if the quantity of such substance in such food does not ordinarily render it injurious to health; or * * * (3) if it consists in whole or in part of any filthy, putrid, or decomposed substance, or if it is otherwise unfit for food; or (4) if it has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health; * * * or, (6) if its container is composed, in whole or in part, of any poisonous or deleterious substance which may render the contents injurious to health.

Recently I sought to amend subsection (3) so that it would read as does (1), as follows:

If it consists in whole or in part of any filthy, putrid, or decomposed substance; but in case the substance is not an added substance such food shall not be considered adulterated under this clause if the quantity of such substance in such food does not ordinarily render it injurious to health.

The reason for that amendment is disclosed in hearings not yet printed which were held by a subcommittee of the Committee on Expenditures in the Executive Departments. Those hearings were held in Michigan. Growers, processors, and representatives of the food and drug department of the State of Michigan appeared and testified.

I have been advised that Michigan cans three-quarters of the canned black raspberries of the country. Black raspberries, red raspberries, and blackberries, and many other berries and fruits, as they grow in the fields or orchards, have mold in them, but the mold is not injurious to health. So I proposed an amendment as just outlined; this came up after the Department had seized quantities of this canned product, which they admitted was not harmful, was not injurious, was a wholesome, tasty food. I proposed an amendment which would prevent seizure, and if there was mold in the berries as processed, they were not to be seized, not to be declared unlawfully sold, if they were not injurious to public health, and I tried to get the Department to establish a standard; that is, a rule or regulation which would declare what percentage of the product could show mold without being subject to seizure. The State authorities did establish a percentage of 75 percent, I think it was. That does not mean that 75 percent of the product was moldy. It means that in 75 percent of the areas they could, under a microscope, discover mold. They could not smell it or taste it, but when they put a microscope on it they could find a little something there that indicated mold. They made no claim that the mold on the product was unwholesome or injurious or distasteful. So if a canner did not just walk the chalk line, if he was a little hurried in having to get the berries through the factory and did not use as nice words as the inspector thought he ought to, the product could and would be seized, as inspectors had been doing. In one instance the Department agent seized the produce; and they did, some $3,700 worth in one instance, admitting all the time that it was not injurious to anyone and that no one could learn there was mold in it except as they put a microscope on it. The State gave us relief; that is, the State of Michigan established a standard of tolerance for mold, but did these fellows down here? They would permit some mold, but how much? Would they tell the growers or the processors? No, sir; not on your tintype. And along comes this fellow from the Department, Deputy Administrator George Larrick who apparently would not know a raspberry from a pumpkin, and spills himself in the paper thusly——

The CHAIRMAN. The time of the gentleman from Michigan has expired.

Mr. HOFFMAN of Michigan. Mr. Chairman, I ask unanimous consent to proceed for five additional minutes that I may finish this story.

The CHAIRMAN. The time has been fixed.

Mr. HOFFMAN of Michigan. Then I offer a motion to strike out the enacting clause.

The Clerk read as follows:

Mr. HOFFMAN of Michigan moves that the Committee do now rise and report the bill back to the House with the recommendation that the enacting clause be stricken.

The CHAIRMAN. The gentleman is recognized for 5 minutes in support of his motion.

Mr. HOFFMAN of Michigan. Referring to my attempt to obtain an amendment to the legal definition of adulterated food as carried in section 342 of title 21 of the Code, which would enable growers, processors, and retailers to put a tasty, wholesome, noninjurious food—the black raspberry crop—in the hands of consumers when I proposed an

amendment to subsection 3 of section 342, practically identical language to subsection 1, he apparently gave a reporter of the Washington Daily News an interview for the News of that date. Referring to that amendment the reporter writes:

Bugs baked into cake, catsup made with spoiled tomatoes, and moldy raspberries—all will be on your dinner table one day if a bill introduced by Representative CLARE E. HOFFMAN, Republican, Michigan, becomes law.

The bill would amend the Federal Food, Drug, and Cosmetics Act to allow food to be marketed with "filthy, putrid or decomposed" matter as long as the matter is not "added" and would not be "injurious to health."

At least this was the interpretation of Deputy Food and Drug Administrator George Larrick when asked about the bill today.

Even so, "The way it reads bakeries could make cake with contaminated flour—with bugs and rodent hairs and some of the other things we find—without our being able to do anything about it," Mr. Larrick said. "The baking processes would kill any harmful bacteria and make it technically uninjurious."

Now, the attitude taken by this gentleman illustrates the all too often arbitrary, unreasonable position and misleading statements put out by the Department spokesmen every time anyone ventures the thought that perhaps the Department's employees, and that is what they are, might just possibly not know everything that is to be known, should not be trusted with the opportunity to injuriously destroy whole sections of our economy.

I never heard of anyone who wished to use or have others use filthy, putrid or decomposed food as those words are commonly understood. Nor did I ever know of anyone who wanted to make it possible for a grower, a processor or a retailer to induce a consumer to purchase a food which was not what it was represented to be.

Permit me now to give you an illustration of just how untruthful and I might add, knowingly untruthful if he has any intelligence at all, is this Deputy Administrator George Larrick, if he is correctly quoted. The press carries this quotation from him:

The way it—

Meaning the amendment—

reads—bakeries could make cake with contaminated flour—with bugs and rodent hairs and some of the other things we find—without our being able to do anything about it.

The absurdity of that statement, its falsity, is apparent on its face. Certainly Mr. Larrick knows that flour containing bugs, rodent hairs and the other things to which he refers has had something "added to it," or is he so set in his ways that he is trying to make us believe that bugs and rodent hairs are a part of the wheat as it grows—as mold is a part of black raspberries as they grow and as the State health authorities of Michigan have recognized?

This one illustration just given and which is Mr. Larrick's and the Department's only contribution to a situation which exists in Michigan where growers of nutritious, wholesome berries—where processors who at the cost of thousands of dollars have hired State and other inspectors—skilled chemists, microscopic experts, who have sterilized all receptacles used to collect berries from the time they are picked until they reach the processing machinery, are trying to lower the cost of living by putting a product on the market where otherwise it would either be not grown or wasted. Black raspberries as grown carry mold as does the air we breathe, at least that is the testimony of the experts—the experts told us that the moment one of the little droplets breaks down the berry is "decomposed," or it has started to rot. The same experts assert that this mold is not harmful, that it may even, like penicillin, be a curative mold.

But the Department all blown up by its own conceit, acknowledging the healthfulness of the product, will not establish a mold standard so that farmers may be encouraged to plant and grow the berries, so that processors may handle them, and the rest of us have available at reasonable cost a delicious, nourishing food or dessert.

Taking note of the above, perhaps you can get a dim idea of just how unreasonable and arbitrary some of these gentlemen may be. It is possible that it is this arbitrariness, this unreasonableness, on the part of these gentlemen in the Department that frightens the gentleman from North Carolina [Mr. BONNER].

Did anyone here ever eat a beefsteak which was not decomposed?

In *A. O. Andersen & Co. v. United States* (234 Fed. 542) the Ninth Circuit Court of Appeals, said:

Decomposition may begin where life ends, but meat or fish is not decomposed at that early stage. Decomposed means more than the beginning of decomposition; it means a state of decomposition, and the statute must be given a reasonable construction to carry out and effect the legislative policy or intent.

Do the gentlemen of the Department ever gracefully accept a reasonable ruling of the courts such as that which has just been quoted? Oh, no.

Processed black raspberries are decomposed whenever Mr. Inspector has a grouch.

Black raspberries, as they mature, have mold in them, and as they ripen some of the little cells containing the substance of the berries inevitably break down. Those cells are decomposed—they are rotten, but until they have reached an advanced stage of decomposition, or where the mold is excessive, they are tasteful and nutritious—but will the Department let them pass? Not if the inspector got out on the wrong side of the bed or if his breakfast did not agree with him, or if someone has not treated him with proper deference.

These gentlemen down here say that if there is any mold, if there is any decomposition, even though it does not hurt anyone, the product is rotten. Did anyone ever eat a piece of cheese where, somewhere along the course of its manufacture, it did not contain decomposed milk? No; of course, you did not; and blue cheese—the more mold there is in it the better. And penicillin. Do they object to that?

But if you can with a microscope find a little bit of mold in a berry it should not be sold. So the United States Department tells the grower, the processor.

Does that mean anything? Yes; I have here an article in our local newspaper where the berry grower says that his whole crop when put on the market brought a price of $1.60 a crate—this was just last week. It cost him $1.50 a crate to pick, package and deliver. He did not count his work in growing, in spraying, in cultivating nothing for investment. So he said to the folks "Come in if you want berries; you pick them, but bring your own containers." He did not propose to furnish containers. And growers are forced out of business—processors just turn to other fruits or vegetables. The consumer has his supply cut short.

Now, what is the Drug and Food Department down here doing? They are taking off of the local processing market tons and tons of wholesome berries and fruits because the processors will not take the risk, will not can this crop when they know that at the whim of some bureaucratic agent down here it is subject to seizure. If they would give us a tolerance for mold it would be all right; but, no, they will not do it; they want to go around the country and show their authority.

Yet the berries which our local processors cannot handle are often sold at a lesser price to processors from Detroit or Chicago who process them and put them on the market, without fear of seizure. Moreover, if not bought by processors some of this fruit, but at a lesser price goes on the fresh market, is bought and used by the housewife—as critical but at the same time reasonable an inspector as ever bought a food product or condemned a food.

Mr. O'HARA. Mr. Chairman, will the gentleman yield?

Mr. HOFFMAN of Michigan. I yield.

Mr. O'HARA. Did I understand the gentleman to say that not only are they mistaken but they are arbitrary? Is that a correct quotation?

Mr. HOFFMAN of Michigan. Arbitrary. Brother, you have never seen anything until you have seen these gentlemen and the agents from the Labor Department who go into the factories and tell all the workers that they are working too hard for too little money, producing too much—making trouble. Stalin's agents never were able to stir up as much discord in this country as the agents of some of these departments, whose heads swell out of all proportion the moment they get a badge. That is why I do not want to give an administrator this arbitrary authority.

Mr. SMITH of Wisconsin. Mr. Chairman, will the gentleman yield?

Mr. HOFFMAN of Michigan. I yield to the gentleman from Wisconsin.

Mr. SMITH of Wisconsin. Are we to infer from what the gentleman has said that he has no confidence in Oscar Ewing?

Mr. HOFFMAN of Michigan. I would not want to express an opinion on Oscar at this time. I heard him testify once it was not only his right but duty to use Federal funds to spread the gospel as he interpreted it to the people of the country, although I know there is a

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statute which makes it a criminal offense to do that with Federal funds.

The CHAIRMAN. The time of the gentleman from Michigan has expired.

Mr. HOFFMAN of Michigan. Mr. Chairman, I ask unanimous consent to withdraw my motion.

The CHAIRMAN. Is there objection to the request of the gentleman from Michigan?

There was no objection.

The CHAIRMAN. The question is on the amendment offered by the gentleman from Alabama [Mr. ROBERTS]

The amendment was agreed to.

Mr. O'HARA. Mr. Chairman, I offer an amendment.

The Clerk read as follows:

Amendment offered by Mr. O'HARA:

Page 5, strike out lines 6 to 16, inclusive, and insert in lieu thereof the following indented paragraph:

"(B) because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, is not safe for use except under the supervision of a practitioner licensed by law to administer such drug; or."

On page 7 strike out line 13 and all that follows down through line 25 on page 8.

On page 9, line 1, strike out "(6)" and insert "(5)."

Mr. O'HARA. Mr. Chairman, I ask unanimous consent to proceed for 10 additional minutes.

The CHAIRMAN. Is there objection to the request of the gentleman from Minnesota?

There was no objection.

Mr. O'HARA. Mr. Chairman, I have asked for additional time so that I might fully explain what this amendment does to the pending bill. Let me say that it represents the controversy which lies between the majority side and the minority side of the committee upon this bill.

Mr. WILLIAMS of Mississippi. Mr. Chairman, will the gentleman yield?

Mr. O'HARA. I yield to the gentleman from Mississippi.

Mr. WILLIAMS of Mississippi. I wish the gentleman would not say "minority side." I wish he would tell the truth and say "minority of the minority of the committee."

Mr. O'HARA. If the gentleman is going to be technical, may I say I have been on a minority of 9 out of 435, yet my position was sustained in the other body and became law. I do not know what a minority is any more, but I have been in the minority many times. The gentleman has repeatedly stated that the vote was 4 to 19. I am happy to be one of those 4. I would be happy to be 1 if I thought I was right.

Mr. Chairman, I should like to proceed and tell you exactly what this amendment does.

First it corrects subsection (B) and takes all of this confusing language out that so many Members have talked about and puts it in simple language, it gives the Administrator all the authority in the world for the protection of the public and enforcement of the law as to the safety of the public that he can possibly ever need without the uncertainty of these experts and all of that which is in the committee amendment.

Mr. BENNETT of Michigan. Mr. Chairman, will the gentleman yield?

Mr. O'HARA. I yield to the gentleman form Michigan.

Mr. BENNETT of Michigan. Those in charge of the administration of this law some 10 years ago, in 1941, agreed with the position now taken by the gentleman from Minnesota. At that time it issued a directive or memorandum—I do not know what you would call it—with respect to defining and listing prescription drugs. This is what it says:

The Administration—

That is the Food and Drug Administration—

has received numerous requests from drug manufacturers, retail and wholesale drug associations, and others, for a list of those drug products which it considers dangerous when sold otherwise than on the prescription of a physician, dentist, or veterinarian licensed by law to administer drugs.

In answer to such requests, the Administration has pointed out that the Food, Drug, and Cosmetic Act places upon the manufacturer and the distributor the responsibility for properly safeguarding the marketing of drugs which may be dangerous to the purchaser if distributed without restriction. Obviously, it is impossible to list all drugs which may be dangerous since not only the compositions but also the directions for use and the conditions in which their use is recommended may have a very definite bearing on the question of safety or danger.

That was their decision 10 years ago.

Mr. O'HARA. That they could not make such a list as they now claim they can, of 30,000 drugs.

Mr. BENNETT of Michigan. And with an additional 3,000 since.

Mr. AUGUST H. ANDRESEN. Mr. Chairman, will the gentleman yield?

Mr. O'HARA. I yield to the gentleman from Minnesota.

Mr. AUGUST H. ANDRESEN. Of course, at that time they did not have Oscar Ewing running the show.

Mr. O'HARA. That is true. There is no question but what the amendment to subsection (B) is plain and broad and gives the Administrator all the power he needs. I wish you would turn to that portion which my amendment strikes out, commencing on line 13, page 7. Here is what the bill gives to the Administrator and what goes on if he makes these 30,000 decisions, or any part of them. Someone, of course, has the right under the bill—they call this protection—to start in then and object to what is done. All right. The first thing the Administrator does is to give notice after the objector has filed objections to that classification. Thereafter the Administrator makes public his action on the proposal. Then, No. 3, within 30 days after such action the interested party may file with the Administrator his objections, stating the changes proposed, and all of the other things that he has to go through. No. 4: Then the Administrator shall give notice and hold a public hearing. No. 5: Then the Administrator shall make a determination and issue an order. If summons and petition is served on the Administrator, the Administrator shall certify and file in the court the transcript of the evidence and then the poor fellow is finally in the Federal court of appeals.

But, what is he up against under this bill? He is up against this situation. No. 1, the burden of proof has been shifted from the Administrator to the person affected. No. 2, he is up against this impossible situation, and any of you who are lawyers know what it means to appeal from a finding of fact by a court or administrative body; he is up against this provision of the law:

The findings of the Administrator as to the facts, if supported by substantial evidence, shall be conclusive.

Now, that means that, under this bill, if you were opposing some order that was made as to what this drug was a prescription or nonprescription drug, the Administrator, under the decisions of the courts, both as to the Food and Drug Administration and the Federal Trade Commission and these various administrative agencies, can call in an expert. Under the decision, even if that expert is biased, and the reviewing court says he was biased, they still must affirm that finding. Now, that is a perfectly ridiculous situation to give this tremendous power to Oscar Ewing. I like Oscar Ewing personally; I like his frankness. He is for socialized medicine. He has stated so on two or three different occasions before our committee.

Mr. DONDERO. Mr. Chairman, will the gentleman yield?

Mr. O'HARA. I yield to the gentleman from Michigan.

Mr. DONDERO. Does that mean that the ordinary individual, a doctor or pharmacist or druggist, is denied his day in court? Is that what it means?

Mr. O'HARA. That is what it means.

Now let me pursue it further. I admire Oscar Ewing for his frankness and honesty. On at least two, possibly three, occasions I heard him say that the medical expenses of the people of this country should be paid for by the Government, whether the people who incurred the medical expense are in a position to pay or not. He has repeated that on two or three different occasions. He has written a book, which is a blueprint, in my opinion, for the program of socialized medicine, and we fought all last year in our committee, practically, over the so-called socialized medicine bill. His book is entitled "The Nation's Health: A Ten-Year Program—A Report to the President by Oscar R. Ewing, Federal Administrator," and printed at Government expense. Seventy-five thousand copies have been circulated in the country.

As to this delusion about the Administrator not having authority, there is absolutely no question that if there is any mislabeling of drugs or misrepresenting to the public of drugs which have not been passed upon and approved, the Administrator has all the power in the world to prosecute those people both criminally and civilly, civilly by seizing the drug and criminally by prosecuting them for violation of the law.

Mr. HARRIS. Mr. Chairman, will the gentleman yield?

Mr. O'HARA. I yield to the gentleman from Arkansas.

Mr. HARRIS. Is it not true that we had testimony before our committee which showed that a certain type of

chalk made by one manufacturer had one label on it when they sent it to the druggist and when it was made by another manufacturer it had another label on it? Would it not be true that if this provision that is proposed here were to prevail, the Administrator would have the right to see that the manufacturers had to label that item properly?

Mr. O'HARA. There is no question that under the law today and under my amendment he would have a right if that article was mislabeled to prosecute those people, but as to this mislabeling of chalk, some kind of chalk, I have forgotten what it is called, a perfectly harmless drug, it is true that some drug manufacturers manufacture to sell over-the-counter products and other manufacturers sell and want to sell only to physicians and druggists for prescription use. There is a difference in the viewpoint of the drug manufacturer. I do not see that there is anything confusing about it. I think all this talk about these little items, because there are a few items where one drug manufacturer takes one view, and another a different one, is not important. I do not like the confusion but I do not think it amounts to anything.

Mr. HARRIS. I believe the gentleman will have to admit it does amount to a lot, because if one of the antibiotics, for instance, were involved it would have a tremendous effect on the health of the people.

Mr. O'HARA. Is any claim made on the gentleman's part that any antibiotics are mislabeled? Is there? The gentleman is talking of a few items of drugs that do not amount to a great deal.

Mr. HARRIS. I am sure the gentleman will recall when a few years ago these sulfa drugs first came out, and many, many people throughout the country died as the result of their use.

Mr. O'HARA. Yes; it may be that that is true, but they were approved by the physicians, they were approved by the Food and Drug Administration, and it was not because the Administrator did not have the authority to do something about it.

Mr. MASON. And they were not mislabeled.

Mr. O'HARA. They were not mislabeled. They were told exactly what they were. However, the reaction was not known as definitely as it developed later, and they did not know what should also be administered. That was the point.

Mr. HALLECK. Mr. Chairman, will the gentleman yield?

Mr. O'HARA. I yield to the gentleman from Indiana.

Mr. HALLECK. In respect to the alleged need for this section to which the gentleman refers in this legislation, I am informed that Mr. Larrick, Associate Commissioner of the Food and Drug Administration, testified before the House committee in these words: "The present law, so far as it has been interpreted, is sufficient to protect the consumer."

Mr. O'HARA. I know there is no question about it. The consumer and the public are amply protected under present law. What is being attempted here is to give this terrific amount of power to Oscar Ewing and the Food and Drug Administration to bring about a complete change in the entire picture in this country. Let me say to you, and I say it in all seriousness, that this bill, at least as it is now written, is the handmaiden of socialized medicine.

Mr. KEARNS. Would the gentleman explain whose brain child this bill is? That is the thing I cannot find out. Where did it originate?

Mr. O'HARA. The first time I heard of it was when I heard of the Humphrey-Durham bill.

Mr. HALLECK. Mr. Chairman, will the gentleman yield?

Mr. O'HARA. I yield.

Mr. HALLECK. As I understand it, the bill as originally introduced did not have this controversial section in it.

Mr. O'HARA. The gentleman is correct, I believe.

Mr. HALLECK. It had to do with telephone prescriptions and the refilling of prescriptions.

Mr. O'HARA. That is right, and we are leaving all of that in the bill.

Mr. HALLECK. When the druggists back home write us, as some have written to me to tell us to be in favor of the Humphrey-Durham bill do they have in mind the bill originally introduced which did not include this controversial section?

Mr. O'HARA. I cannot assume that they do. I know some of my colleagues have sent them copies of the bill and they have said "We do not want that bill." That is all I know. They say "We do not want that part of it."

Mr. HALLECK. I received one letter where the druggist wrote me "This bill enables pharmacists to fill and refill prescriptions according to their ethical and professional training which after all is the best judge in such matters." Would that particularly have reference to the filling and refilling section of this bill?

Mr. O'HARA. That is my interpretation of it. That is what I have heard from all of the druggists that have contacted me and that is what they are interested in.

Mr. HALE. Mr. Chairman, will the gentleman yield?

Mr. O'HARA. I yield.

Mr. HALE. If the gentleman will look at page 2 of the bill, lines 16 to 20, he will observe these provisions giving wide powers to the Administrator were in the bill as originally introduced.

Mr. O'HARA. I spoke of the original bill. That is the gentleman's interpretation of the last bill. We may be correct. I think the gentleman was as anxious as I was to strike those powers out. I think he felt they were too broad.

Mr. HALE. Yes; but in the interest of accuracy I think it should be said that the original Durham bill did confer powers on the Administrator which were of quite wide nature.

Mr. O'HARA. I do not believe section 5 was in the original bill, before us.

The CHAIRMAN. The time of the gentleman from Minnesota has expired.

Mr. O'HARA. Mr. Chairman, I ask unanimous consent to proceed for two additional minutes.

The CHAIRMAN. Is there objection to the request of the gentleman from Minnesota?

There was no objection.

Mr. BONNER. Mr. Chairman, will the gentleman yield?

Mr. O'HARA. I yield.

Mr. BONNER. There is a question I would like to clear up in my mind and that is whether the original Durham bill carried the vast power that this bill carries.

Mr. O'HARA. In my opinion it did not. There was some provision on page 2 which gave him additional powers but not the broad powers that are contained in subsection 5.

Mr. BONNER. Did Mr. DURHAM testify before the committee for the bill as is?

Mr. O'HARA. He has not had an opportunity to testify to it as the bill was reported out—of course not—because it was amended and these additional powers, both subsection (b) was amended and subsection 5 as I recall it, was added. That was after we had several days of executive consideration and after the gentleman from Mississippi suddenly appeared with what I assume was the brain child of the Food and Drug Administration and the retail druggists association.

Mr. DONDERO. Mr. Chairman, will the gentleman yield?

Mr. O'HARA. I yield.

Mr. DONDERO. This is the fourth Durham bill and not the first one or the second one, is that correct?

Mr. O'HARA. I think that is correct. The first one we had hearings on was the bill as introduced; not the amended one which we have before us.

Mr. WILLIAMS of Mississippi. Mr. Chairman, will the gentleman yield?

Mr. O'HARA. I yield.

Mr. WILLIAMS of Mississippi. I just want to straighten the gentleman out on that. He knows I am not going to kowtow to Mr. Ewing or any of his subordinates. I just want to tell him that the amendment was worked up by the staff of the committee with my assistance, or worked up by me with the assistance of the staff of the committee, whichever way you want to put it, to carry out the purposes we thought the Committee on Interstate and Foreign Commerce wanted to accomplish.

Mr. O'HARA. I fear the Food and Drug people worked very closely with the staff—perhaps not with the gentleman—but they worked very closely with the staff.

Mr. Chairman, I hope this amendment will be adopted because it determines whether you want this administrative absolutism or whether you want to continue in the American way in this important problem.

The CHAIRMAN. The time of the gentleman has expired.

Mr. HARRIS. Mr. Chairman, I rise in opposition to the amendment.

Mr. Chairman, I am opposed to this amendment. The gentleman from Minnesota [Mr. O'HARA] strikes at the very heart of this bill. This is the crux of the issue. It is the real issue before this Congress and before the American people.

It is a rather interesting thing when Oscar Ewing is being used as a whipping boy here. I will say to you if his name was not involved in this legislation you would not have a leg to stand on, and you know it. You drag out before this Committee the thing that you think will create the most prejudice against a piece of good legislation. I doubt if there is any Member of this House who has opposed Mr. Ewing in his proposal to socialize the medical profession and the health of our people.

Mr. HALLECK. Mr. Chairman, will the gentleman yield?

Mr. HARRIS. I yield to the gentleman from Indiana.

Mr. HALLECK. The gentleman knows my high regard for the gentleman from Arkansas. I have a letter here from the executive secretary of the National Association of Retail Druggists, whom I know and like very much. I suppose everybody had such a letter. He expresses support of the bill. But, in the final paragraph, on the first page, he says:

> The second purpose of the bill and the one of great immediate concern to druggists is to relax the present unrestricted provisions of law regulating the filling and refilling of prescriptions.

If that is of great concern to the druggists, then how can you say if this amendment were adopted it would strike at the heart of the bill?

Mr. HARRIS. Everyone is in accord with reference to the necessity, the imperative necessity of correcting the present law with reference to the refilling of prescriptions and of telephonic prescriptions. Everyone is agreed on that. The other issue is this one, which I repeat, is the crux and the real issue before this House. I said before that this is the issue; it is a fight between the commercial manufacturers of drugs and the retail druggists throughout the country as to what the best way and where the responsibility should be on safe drugs dispensed by prescription.

In all deference to everyone in this House, the manufacturers of drugs have raised a big bug-a-boo here about Oscar Ewing, and you are attempting to defeat a very worth-while cause that the commercial interests are against, by using what some would say is an unpopular Administrator to do that. Now, let us get the cards face up on the table. I think the membership is entitled to know. The gentleman from Maine [Mr. HALE] told you a moment ago what the facts were with reference to this legislation. Before I leave it, however, I would like to say to the gentleman from Indiana [Mr. HALLECK], if he will read page 2 of the letter from Mr. Dargavel he will observe that he devoted three paragraphs to this issue, in which he said:

> The sole opposition to the bill is from the manufacturers of drugs and their satellites. The Proprietary Association is the most active. The spokesmen of this organization argue that the authority to decide which drugs must be sold on prescription only should be lodged exclusively with the manufacturers despite the fact that the Federal Security Agency is charged with the enforcement of this important public law. Instead, the manufacturers wish to leave to case-to-case prosecutions for misbranding the question whether a manufacturer made a proper choice in restricting a drug to prescriptions or in deciding to have it sold over the drugstore counter.
>
> The burden of compliance falls upon the druggist as well as upon the manufacturer. We do not wish to be made criminal defendants or to have drugs on our shelves seized for the purpose solely of obtaining an authoritative decision whether the drug should in the future be sold on prescription only or should be over the counter. We believe that is the kind of question that should be settled in advance, and we have confidence that the Food and Drug Administration of the Federal Security Agency is competent to make the determinations. The bill provides the same safeguards against abuse of the administrative power that Congress provided in the Administrative Procedure Act after the most careful study of the question.
>
> The patent medicine manufacturers argue that H. R. 3298 involves life or death to them. We answer that failure to enact the bill will spell life or death for an untold number of people. Death can, indeed, result from the over-the-counter sale of many drugs. This bill is designed to prevent injury to the public health, and we believe that it should be passed at the earliest possible time.

Mr. BELCHER. Mr. Chairman, will the gentleman yield?

Mr. HARRIS. I yield to the gentleman from Oklahoma.

Mr. BELCHER. I do not know who Mr. Dargavel is.

Mr. HARRIS. He is executive secretary of the National Association of Retail Druggists.

Mr. BELCHER. I do not know who he is, but he does not speak for the druggists of the Eighth Oklahoma District, because I have had wires from them opposing this bill.

Mr. HARRIS. I appreciate the gentleman's position.

The gentleman from Indiana [Mr. HALLECK] brought up the letter of the executive secretary, representing the National Association of Retail Druggists, and that is the reason I referred to it. I assume he speaks for the 35,000 retail druggists throughout the country. Everyone to his own feeling.

The gentleman from Indiana asked a question a moment ago of the author of this amendment, to the effect that the original Durham bill did not have this provision which he proposes to strike out.

Let me say to the gentleman from Indiana and Members of this House, if you will turn to page 2 of this bill, you will see that language stricken out. That is in the bill proposed by the gentleman from North Carolina [Mr. DURHAM], and you will notice that language is much broader and had far-reaching consequence which this bill does not have.

In the course of the consideration of this legislation in the committee the gentleman from Maine offered some amendments. Those amendments would in effect do just what the gentleman from Minnesota proposes to do now. The committee adopted those amendments.

After their adoption and we began looking into the effect and result then we came to a determination that it would not do what was proposed originally and what the committee felt was necessary to correct or adequately adjust the Food and Drug Act; so the committee reconsidered the entire amendment that had been offered by the gentleman from Maine and we took the standards that were set up to tie the hands of the Administrator and provided them here in (a) (b) (c), (b) and (c) are the two paragraphs here, (b) being the one in controversy that sets a standard by which the Administrator must obviously act in accordance with the administration of this program. It ties the hands of the Administrator where he must follow the standard set up and consequently does not give him the broad unlimited authority that some would have you believe today.

Mr. EVINS. Mr. Chairman, will the gentleman yield?

Mr. HARRIS. I yield.

Mr. EVINS. The gentleman says in one breath that we give the Administrator authority and then in the next breath he says we tie his hands. If the pending amendment is adopted it will not be necessary.

Mr. HARRIS. No, it will not be necessary; but you will leave—and if the committee wants to do it, it is all right—you will leave to the authority of the commercial drug interests in this country to decide in all instances what is best for the American people and the health and welfare of the people. There is the crux of it today.

All these patent medicines are involved, and there is some confusion because of the technicality as to what this would do. But let me say to the gentleman again that this would have no adverse effect whatsoever on any accepted patent medicine that is on the market today.

Mr. SCRIVNER. Mr. Chairman, will the gentleman yield?

Mr. HARRIS. I yield.

Mr. SCRIVNER. It is a little hard for me to understand why you give a man such power as you say is given here and then tie his hands. Why give him the power in the first place?

Mr. HARRIS. For the simple reason that because of all of these new medicines and drugs that come on the market almost daily the committee felt there should be some determination by somebody as to whether or not they were safe drugs and should be dispensed by prescription or sold over the counter.

This is relief for the retail druggists who have the responsibility as much as the commercial industry in the determination of these drugs.

I will say to the Committee that I think it could very well be to the best interests of the American people if this amendment were defeated.

Mr. DOLLIVER. Mr. Chairman, I rise in support of the amendment.

Mr. Chairman, I should like to discuss this matter objectively and dispassionately. I sat through the hearings on this legislation for a good many days. I believe I heard every word that was uttered about this legislation in the committee, both in public and private sessions.

It is not a simple piece of legislation and I am sure that some of you who have listened to the debate this after-

noon may be somewhat confused about it.

I would like you to know, first of all, that there are important parts of this legislation which are not controversial, and I use the word "important" advisedly. Those important parts are contained in the last part of the writing on page 5, beginning about line 21, and going over to about line 3 on the next page. They refer to the oral prescriptions and the refilling of prescriptions. That, really, is the important part of this legislation from the standpoint of the people who are affected by it.

Mr. MASON. Mr. Chairman, will the gentleman yield?

Mr. DOLLIVER. I yield to the gentleman from Illinois.

Mr. MASON. I would prefer that those things be called the sugar-coating to get us to swallow the part of the bill that most of us do not want.

Mr. DOLLIVER. We can rectify the situation to which he objects by adopting the amendment which is now under consideration by the committee. That is exactly what should be done.

Mr. MASON. I agree with that.

Mr. MORANO. Mr. Chairman, will the gentleman yield?

Mr. DOLLIVER. I yield to the gentleman from Connecticut.

Mr. MORANO. The distinguished gentleman from Arkansas said that if we adopt this amendment we would strike out the heart of the bill. Will the gentleman from Iowa comment on that?

Mr. DOLLIVER. I disagree with the gentleman from Arkansas. This is not the heart of the bill. It is one of the issues, to be sure, but it is not the most important part of the bill from my standpoint at least.

What is the argument about with reference to the amendment offered by the gentleman from Minnesota [Mr. O'HARA]? It is whether you are going to turn over to the Social Security Administrator, Mr. Ewing, at the present time—but I would not care whether it was Mr. Ewing or someone else—certain authority to proscribe certain drugs.

I want to be fair about Mr. Ewing. I know from his testimony before the committee that he did not ask for this authority. I heard him say so in the hearings. He has not asked for this power. But he has asked, and everybody who is interested in this legislation is asking for those parts I referred to in the beginning of my statement, clarification of the situation with respect to oral prescriptions and with respect to refilling of prescriptions.

We are now arguing about another matter which, to be sure, is important. In my honest opinion, we ought to adopt the amendment offered by the gentleman from Minnesota [Mr. O'HARA] because thereby we would get a bill which would be acceptable, as I see it, to most of the people who are interested in this and would continue the kind of protection to the general public which it now enjoys under the Food, Drug, and Cosmetic Act.

If it should transpire in the future that what we do in adopting the O'Hara amendment is not satisfactory; if it does not complete the task, why, of course, the Congress will be in session, there will continue to be a Committee on Interstate and Foreign Commerce to take up this matter. We can rectify the situation.

But as of now it is my considered judgment, and I hope the considered judgment of a majority of this House, that we should adopt the O'Hara amendment, and pass the bill in the form that it ought to pass. We will do no one harm in so doing—as we might very well do if it were passed without the amendment.

The CHAIRMAN. The time of the gentleman from Iowa has expired.

Mr. THORNBERRY. Mr. Chairman, I move to strike out the last word.

Mr. Chairman, I would like to discuss the pending amendment as calmly as possible.

There are two reasons why I am opposed to the O'Hara amendment. In the first place, it leaves the retail corner druggist in the same position that exists today under the present law. Under the present law he does not know whether the drugs that he sells over the counter are in violation of the law until the Food and Drug Administrator comes and seizes the goods on his counter or files a criminal complaint against him. You can realize that when goods are seized on his counter his standing in the community is hurt. The second reason I am opposed to the O'Hara amendment is that, in my opinion, it does not give the protection to the public which is needed. We hear the cry of socialism and of strong centralized power, but the Food and Drug Administration has the same power given to it in this bill, on habit-forming drugs and on new drugs. Nobody has said anything about those powers, but when we come to try to correct the situation about drugs that are dangerous to human beings, then we hear that it is too broad a grant of power. What are we going to do about people who somehow or other are entitled to protection against dangerous drugs? Are we going to leave it to a system that the Food and Drug Administrator cannot correct until he comes and seizes the goods or files a criminal complaint? Are we going to correct the situation by a case by case determination? That is what the O'Hara amendment would do.

Mr. WILLIAMS of Mississippi. Mr. Chairman, will the gentleman yield?

Mr. THORNBERRY. I yield to the gentleman from Mississippi.

Mr. WILLIAMS of Mississippi. As I understand, there are 35,000 different drugs on the market. This means that if you adopt the O'Hara amendment the only way the druggist can be certain that he is not selling a prescription drug over the counter is after 30,000 lawsuits have been finished.

Mr. THORNBERRY. That is right. But we do not know how many of these dangerous drugs will be sold over the counter and what are safe for human consumption.

Somehow the Food and Drug Administrator should have the same power with reference to dangerous drugs that he already has with reference to habit-forming drugs and new drugs. Let us not overlook the very point that we are trying to protect the people of America against the use of dangerous drugs. If you adopt the O'Hara amendment, you will leave the retail corner druggist and the pharmacist at the mercy of the Food and Drug Administrator who comes in and seizes his goods and files a case-by-case action in court, either of which is dangerous to him.

Now, there have been a great many statements made here about the retail druggist and how he stands. When the committee report was published I sent a copy of it to every druggist and pharmacist in my district, calling attention to the majority and the minority report, asking them to read them carefully, and I heard from no one of them as being opposed to the bill. Strangely enough, most of the people I heard from were pharmacists who are also druggists, who feel that a change should be made in the law as it exists today. They protest that the present law leaves them at the mercy of either having their goods seized or being hailed into the Federal district court and tried on criminal charges.

Mr. BECKWORTH. Mr. Chairman, will the gentleman yield?

Mr. THORNBERRY. I yield to the gentleman from Texas.

Mr. BECKWORTH. As I said a moment ago, beginning on page 97 of the hearings, you can find more than 100 cases of these small druggists who doubtless, in most instances, innocently were selling drugs. This seeks relief from the kind of situation that the gentleman has just described, nobody knowing about it until after they have committeed the offense.

Mr. THORNBERRY. That is exactly right. And there is not a Member here who will not say that the backbone of small business in our community, for which we plead so eloquently at times, is the retail corner druggist and the small pharmacist who is trying to serve his community. Certainly we should relieve him of the fear of prosecution brought about by an innocent transaction.

Mr. BEAMER. Mr. Chairman, I move to strike out the last word, and rise in support of the amendment.

Mr. Chairman, our very good friend has just given you the "wolf, wolf" cry We have been hearing it so many times from so many people on both sides of the aisle that I hesitate to use it, but I am going to have to yell "wolf," but another kind of wolf.

Let us analyze this situation a bit. There is a system that has been slow in building up, but I tell you it is going to be still slower in deteriorating and much slower in being torn down. I am referring to this system as contrary to the one that you and I want to keep for our own individual initiative, for our own individual responsibility.

Some very good friends of ours, whose opinions I respect and I know you respect, have said very loudly, and I can yell just as loud as they can, if you wish, that the druggists are supporting H. R. 3298.

If the people of this country begin to think for themselves, even including the

druggists, the drug manufacturers, and you and I, if we begin thinking for ourselves and forgetting what the executive secretary of some association, who has some ulterior motive, says, then we are going to get some place.

I did the same thing my good friend from Texas did. I wrote back to the druggists in my district. I know many of these people and have talked to them. I said, "All I want you to do is read the bill and read the committee report." Invariably they wrote back, "We want the refill provision, but for goodness sake, don't help to build up this system that has been engulfing us all the time."

This is called the Durham bill. Read your bill. It has been struck out by the committee. I am sorry, but the estimable gentleman whose name appears on this bill has had a serious operation and is unable to be reached. I have a feeling that with all of his good judgment, which I have heard expressed here today, he would say, "No, this is not my bill."

Mr. BECKWORTH. Mr. Chairman, will the gentleman yield?

Mr. BEAMER. I yield to the gentleman from Texas.

Mr. BECKWORTH. I happen to know the position of the gentleman to whom the gentleman has referred on this very part of the bill. Just prior to the time he left for his operation, he came to my office, and I am sure he went to at least one other office, and he said to me that nothing worse could happen to this legislation than to take out this part of the bill.

Mr. BEAMER. I think it would be very fine if that were a matter of record. So many times today we have asked, "Is this a part of the record?"

I repeat the druggists do not want to sell their birthright for a mess of pottage. They do want a corrected refill provision. You open the door a little tiny bit for some of these bureaucrats—and I will name the Federal Security Administrator—you open the door a little bit and he will walk right in. I said this to the trustees of the American Medical Association and I say it to you today. I can give you an illustration about which you will be hearing. You people from New York State, Tennessee, Florida, and Indiana, you have had experience with this gentleman. You give him an inch and he takes a mile. I am not saying it about the present man because he may be gone tomorrow, but even so this principle still exists.

I say to you it is going to be necessary for you and me to stand up and fight even this little tiny thing. We are going to have to stand up and have the same backbone as these socialistic dreamers. They are doing it. They are not hesitating for a moment, they are not stopping. They are unceasingly on the job. You and I are going to have to stiffen our backs and say, "No, sir. Here is one place we will stop. We will go no further." That is the thing I am trying to impress upon you.

There is one other point I am trying to bring to your attention. Have you heard this expression, "directed judgments"? This committee that the Administrator can set up, supposedly of people who are experts and qualified by experience and training, he can pick, and I challenge you, they have been picked by this administration to choose the proper words and give the proper decisions that will fit the interests of this system that they are trying to build up.

Yes, I am yelling "Wolf," too, and I mean it seriously now. I do not like to yell in this fashion because someday we will have yelled "Wolf" so often that the real wolf will come and not be recognized, but today this is a truly important issue.

Mr. MARTIN of Massachusetts. Mr. Chairman, I move to strike out the last word.

Mr. Chairman, I take this time just for a minute to find out the program for the rest of the week, if I may.

Mr. McCORMACK. If the gentleman will yield, I think that is a very pertinent question and of interest to all Members.

If this bill is disposed of and the rest of the program I had announced for last week is disposed of by tomorrow night, we will go over until Monday. The other bills are the investigative powers outside of continental United States by the Interstate and Foreign Commerce Committee. I do not think that should take very long.

Then, there are two bills from the Armed Services Committee. I understand they are unanimously reported.

There is one bill from the Foreign Affairs Committee.

The only thing that I can see which would hold up action going over from Thursday until Monday would be the unnecessary continuation of the present bill.

Mr. MARTIN of Massachusetts. I thank the gentleman.

Mr. WILLIAMS of Mississippi. Mr. Chairman, I rise in opposition to the amendment.

In order for the House to understand the real difference between the committee's approach to the problem of determining prescription drugs, and that approach which is offered by the gentleman from Minnesota [Mr. O'HARA] in his amendment, I think it might be well for the House to understand, insofar as possible, exactly the problem facing the retail druggist. In understanding that I feel that the House will be in a better position to determine the best vote to cast on this amendment.

I have before me two drugs. These are manufactured by different manufacturers, yet they are identical in chemical make-up, they are identical in quantity, they are exactly the same product. One product is manufactured by the Davies-Rose Co., of Boston, Mass. On this drug—this is quinidine sulfate—you will find this legend:

Caution: To be dispensed only by or on the prescription of a physician.

Here is the same drug manufactured by the Eli Lilly Co., of Indianapolis. There is no legend on this drug.

Mr. O'HARA. Mr. Chairman, will the gentleman yield?

Mr. WILLIAMS of Mississippi. In just 1 minute.

On this drug is written the simple language:

Adult dose: One tablet as directed by the physician.

I yield to the gentleman from Minnesota.

Mr. O'HARA. The gentleman has used this exhibit repeatedly, and, of course, I am familiar with it. Actually, my amendment does not affect section 4, which imposes perhaps some additional responsibilities on the druggist. The gentleman would admit that, would he not?

Mr. WILLIAMS of Mississippi. Not exactly.

Mr. O'HARA. Furthermore, under the present law as it exists today if either of those bottles is mislabeled, the Administrator has every authority under the law to prosecute criminally and civilly.

Mr. WILLIAMS of Mississippi. The gentleman is right up to a point. But in order to see that these prescription drugs are labeled uniformly under your amendment, it would require 30,000 seizures and 30,000 lawsuits on the part of the Administrator.

Mr. HALLECK. Mr. Chairman, will the gentleman yield?

Mr. WILLIAMS of Mississippi. I cannot yield further; I want to complete my statement. If I have time later, I will yield.

Here are two more drugs, identical drugs. On one you will find the prescription legend; on the other you will not find the prescription legend but, instead, the statement:

Average adult dosage, one tablet repeated at intervals of 3 or 4 hours.

This drug is phenacetin. When the retail druggist gets an order from a customer to sell him half a dozen tablets of this drug over the counter and he picks up that bottle and sees that phenacetin manufactured by the Chase Chemical Co. is sitting beside the phenacetin manufactured by Sharp & Dohme—one carrying the prescription legend and the other carrying the dosage label—he does not know whether he is violating the law if he sells that drug over the counter or not. That is what we are seeking to eliminate in this bill.

As to what the amendment offered by the gentleman from Minnesota [Mr. O'HARA] would do—and I may say right here that I know his amendment was offered in good faith; I know the gentleman has worked hard and long on this bill and that he seeks the same as we—relief for the retail druggist and certainty and protection for the public—at the same time I fear that his amendment will not accomplish the end that he desires. He is just taking a different road trying to get to the same destination as we are. The only trouble is that there is a bridge washed out on his road and he cannot get through.

We must put the authority somewhere to determine which drugs are to be considered prescription drugs and which drugs may be sold over the counter.

The druggist, even with the O'Hara amendment, is left right where he was to start with, because in the case of two

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anufacturers of the same drug, one anufacturer says by inference that it a dangerous drug and the other manfacturer says that it is not a dangerous ug. Who is going to determine which anufacturer is right?

The CHAIRMAN. The time of the ntleman from Mississippi has expired.

Mr. WILLIAMS of Mississippi. Mr. hairman, I ask unanimous consent to roceed for five additional minutes.

The CHAIRMAN. Is there objection the request of the gentleman from ississippi?

There was no objection.

Mr. WILLIAMS of Mississippi. The ly way that we can determine which anufacturer is right in such a controrsy is to place the responsibility on meone to determine if—for instance—henacetin, whether manufactured by harp & Dohme or some other chemical mpany is a dangerous or prescription ug. I think there is only one way we n do this, and certainly no other soluon was offered to the committee. The neral definition of drugs which was fered by the gentleman from Minneta does not accomplish the purpose. we do not put that authority in somedy we are not going to help the retail uggist out of the dilemma in which he ds himself because of the confusion lating to prescription drugs.

Mr. HALLECK. Mr. Chairman, will e gentleman yield?

Mr. WILLIAMS of Mississippi. I yield.

Mr. HALLECK. The gentleman rerred to Eli Lilly & Co. They are not in y district, but they are in my State. ey are a reliable concern.

Mr. WILLIAMS of Mississippi. They e a very reliable concern. They are e of the best.

Mr. HALLECK. The gentleman read om that label and said, if I remember correctly: "Adult dosage, one tab-," but the gentleman did not read that also says: "To be prescribed by a physian," or words to that effect. Now, that llows Lilly's policy. What is the matr with that?

Mr. WILLIAMS of Mississippi. If the ntleman read the label on the other ug put out by Davis Rust & Co. he ds this: "To be dispensed only by or the prescription of a physician." On e Lilly bottle it reads: "One or two tabs as directed by a physician." There a lot of difference between the two gends.

Mr. HALLECK. On the Lilly bottle?

Mr. WILLIAMS of Mississippi. On e Eli Lilly Co. bottle the legend is in s language:

One or two tablets as directed by a physian.

To the druggist, that means uncerinty, which is the thing we are atmpting to eliminate through this bill. May I say to the gentleman from Inana that I have had a lot of practical perience in a drug store. As has been d on the floor before, my father was e of the old-time country retail drugts of the State of Mississippi. I have the confusion that comes about as t of these different labels on prepption drugs.

What the druggist is seeking is certainty. I think I know what he wants and needs, and I believe we are going down the right road toward giving that relief with the committee bill.

Now, if the O'Hara amendment is adopted, Eli Lilly & Co. may decide that the drug phenacetin, for instance, comes within the definition of a prescription drug as outlined in the O'Hara amendment. Another drug manufacturer might say that it does not come within that category.

Where does that leave the retail druggist? The only way that the retail druggist can be certain is to have that drug seized, the retail druggist hauled into court, have his drug seized and go through a long, costly process of litigation before some kind of definite determination is made. With 30,000 drugs you can see the impracticability of that approach. The Administrator may simply say that phenacetin is a prescription drug, if he so finds on the basis of testimony of experts as provided in the committee bill and phenacetin, whether manufactured by Eli Lilly, Sharp & Dohme, Squibb, or any other manufacturer, becomes a prescription drug.

If we leave it up to the O'Hara amendment the druggist will need to have a lawsuit to determine whether phenacetin manufactured by Sharp & Dohme is a prescription drug. After he gets that one decided, he will have to have a lawsuit over whether the same drug manufactured by Eli Lilly & Co. is a prescription drug. When he gets that one settled he will have to go on right down the line with the same procedure followed in the case of every company that makes that drug.

Mr. BROWNSON. Mr. Chairman, will the gentleman yield?

Mr. WILLIAMS of Mississippi. I yield to the gentleman from Indiana.

Mr. BROWNSON. In the first place, I do not think the gentleman has been a practicing druggist.

Mr. WILLIAMS of Mississippi. I am not a practicing druggist. I say that I have had practical experience in a drug store. I have jerked soda, hopped cars, and have done about everything but fill prescriptions.

Mr. BROWNSON. Eli Lilly does not sell soda fountain supplies. Their policy is to sell for physicians and for prescription use alone. That is why they indicate one tablet as prescribed by a physician. Does the gentleman want to go further and prescribe how the physician is going to use these drugs in addition?

Mr. WILLIAMS of Mississippi. If the gentleman will get himself a box of Eli Lilly's 5-grain aspirin tablets, he will see that exactly that same legend is put on a box of 500 5-grain aspirin tablets. Why should they put aspirin tablets "One to two tablets an hour as directed by a physician," when the drug is innocuous?

Mr. BROWNSON. Because at the present time Eli Lilly operates on a sales policy of selling for physicians and for prescription use only.

Mr. WILLIAMS of Mississippi. We are not interested in the policies of any individual company. We are interested in protecting the public and providing certainty for the druggist.

Mr. BROWNSON. We are certainly interested in them and I resent the impugning of that reputable firm here today.

Mr. WILLIAMS of Mississippi. The gentleman knows better than to say that. I know that the Lilly Co. is one of the best drug manufacturers, and one of the most ethical. He knows that I am not directing any criticism at that firm. I am merely stating facts.

Mr. HINSHAW. Mr. Chairman, I move to strike out the last word.

Mr. Chairman, I have deliberately moved to strike out the last word instead of rising for or against the pending amendment.

Mr. Chairman, as I told the members of this committee on yesterday, I was not privileged to sit through all of the hearings on this bill nor through all of the hearings in executive session and the consideration of the bill in executive session because of conflicting committee assignments, hence I am somewhat in the same position as most of the members of this committee, only my position is slightly improved by the fact that I was there in committee some of the time.

Mr. Chairman, I think it is quite evident to the members of the Committee of the Whole that the debate here is just about the same as it was in the committee itself. It is just one of those questions that is hard to resolve, and I think that the members of the Committee of the Whole understand, from the telegrams that they have received from retail druggists and from pharmaceutical houses and others, that there is wide interest, and hence wide expression on the part of those people for and against certain provisions of this bill. As a matter of fact, from where we sit it appears to me that this is a piece of legislation that is about to be written by the lobby, and there certainly is not a member of my committee who has had an opportunity to hear any more about them than I, and yet you would act on behalf of the telegrams and letters you have received.

I want to suggest to you one thing. Forget these letters and telegrams that you have received and realize that there are special interests involved here, each one trying to protect its own position, and try to arrive at some solution on the basis of sound reasoning. I will tell you why this committee, in my opinion, was not able to arrive at a unanimous conclusion. I think the reason they were not able to arrive at a unanimous conclusion was because of the lack of strong participation in the consideration of this legislation by the American Medical Society and others who prescribe these drugs. We did not have their advice, to the best of my knowledge, except some belated word that came after the hearings and the executive session consideration, even after the writing of the committee report was concluded.

I think we should have had that advice before we brought this bill here, because certainly the complications of

it are almost too great for any one individual to absorb and come up with a proper judgment.

I think in order to arrive at a right conclusion you are going to have to disregard the letters and telegrams that came to you and think solely and exclusively of the public interest. That is my humble opinion. I hope you will do just that. I am in the same position you are. I know that I am going to have to operate exclusively in the public interest to the best of my ability.

Mr. HARRIS. Mr. Chairman, will the gentleman yield?

Mr. HINSHAW. I yield to the gentleman from Arkansas.

Mr. HARRIS. May I say that I share the sentiments expressed by the gentleman. I would go further and say that the members of the committee sought the information from the American Medical Association, those who would be in charge of issuing the prescriptions.

Mr. HINSHAW. Exactly. We did seek that information and it was not forthcoming, certainly in time to do any good so far as the consideration of this bill was concerned. Nobody can deny that.

Mr. O'HARA. Mr. Chairman, will the gentleman yield?

Mr. HINSHAW. Yes, if the gentleman can deny it.

Mr. O'HARA. We had a communication from the American Medical Association.

Mr. HINSHAW. When?

Mr. O'HARA. While the bill was under executive consideration. The gentleman was not there. It was on June 15.

Mr. HINSHAW. The bill had been written by June 15.

Mr. O'HARA. No, it had not been reported out.

Mr. HINSHAW. It had not been reported out, but it had been written.

Mr. WOLVERTON. Mr. Chairman, will the gentleman yield?

Mr. HINSHAW. I yield to the gentleman from New Jersey.

Mr. WOLVERTON. In answer to the explanation given by the gentleman from Minnesota, I think he is in error. If he would look at the minute book of the committee he would see that at no time did the American Medical Association ever indicate to this committee of ours, opposition to this bill. We sought time after time to have someone representing that organization come before us. I did it myself. It was impossible to get anyone from that organization to appear before our committee. They finally put it off with the idea that it would go before the convention in Atlantic City. The convention was held, and they adjourned without any action whatsoever being taken on this matter.

Mr. BECKWORTH. Mr. Chairman, will the gentleman yield?

Mr. HINSHAW. I yield to the gentleman from Texas.

Mr. BECKWORTH. As I recall, some representative of the American Medical Association was even in the committee room part of the time. He was asked whether or not he would appear, and declined to do so. The committee sought with great diligence to get an accurate expression of the views of the association.

Mr. JUDD. Mr. Chairman, will the gentleman yield?

Mr. HINSHAW. I yield to the gentleman from Minnesota, who, as a physician, ought to know more about this than anybody else around here.

Mr. JUDD. I cannot testify on this particular matter, but I should like to have the benefit of the gentleman's independent judgment as to the merits of this amendment, regardless of lobbies.

Mr. SPRINGER. I would, too.

Mr. HINSHAW. My personal opinion is that it is not as bad as some people would make it out, and with the word "efficacious" stricken out of it by the amendment of somebody here a little while ago, it is perfectly all right. I do not see anything wrong with it as the bill now stands. I am not going to get worked up about Oscar Ewing, either.

Mr. LEONARD W. HALL. Mr. Chairman, I rise in support of the amendment.

Mr. Chairman, it is too bad this bill comes before us today in the form it does. The real question which interests the druggists is the prescription part of the bill. If we could only have passed on that, it would have come out of our committee unanimously, and I think it would have passed this House on the Consent Calendar.

I know there is an association running around saying the retail druggists want this particular part of the bill that the O'Hara amendment strikes out. I have a number of independent druggists in my district, and I have not heard from one of them with respect to that provision of the bill contained in the O'Hara amendment.

I admit there is some confusion. The gentleman from Mississippi has again brought before us bottles of drugs which we saw during the hearings on the bill. I can conceive that maybe our retail druggists are a little bit confused. But I ask you, Are we going to give this grant of power because someone is confused? I have been in this body for about 12 years. I have seen a great amount of confusion on different subjects but I have never seen any of that confusion eliminated by putting more power into the hands of any administrator in Washington. That is just exactly what some members are trying to do here today.

Let us consider the problem presented by these bottles of drugs further: Under the present law the Administrator can correct that today. No one can deny that. But he does not want to go into court and get an injunction. He does not want to proceed by criminal proceedings. He wants to get an administrative court so as to make his job that much easier. Under section 4 of the bill as we have it before us today the Administrator is given even more power to correct the situation on the labels as described by the gentleman from Mississippi.

I am sorry that when we get any piece of legislation we have to go down the same path and admit that there is only one answer, namely, to give somebody more power in Washington.

Apparently we have reached the point where we do not trust our big manufacturers.

Consider the case of aureomycin. Somebody mentioned that the other day. I know a little bit about it. Millions of dollars were spent before that drug appeared on the market. Do you think those manufacturers who are now making great profits are going to put anything on the label of that drug which is not true? For selfish reasons alone they would not. I think we still have to have a little faith in them.

Most of our States have laws on their books with respect to the dispensation of drugs. Have we reached the point where we do not even trust our State governments? To me this in part is a good bill but let us not use the good part of the bill to put more power in the hands of some bureaucrat in Washington.

If we pass this bill today in its present form, and I remind my colleagues that many Members get up on the floor each year and say that we should not give any more appropriations or larger appropriations to heads of bureaus or commissions, I repeat, if we pass this bill today Oscar Ewing is going to come before us next year and is going to say, "I have to list all of these drugs." I think he will have a perfect right to say that he will have to have a number of new employees to carry out the job that Congress has given to him under this bill. Let us not cripple a good and necessary piece of legislation by adding to it this uncalled-for grant of power.

I trust the O'Hara amendment passes.

Mr. KEATING. Mr. Chairman, will the gentleman yield?

Mr. LEONARD W. HALL. I yield.

Mr. KEATING. There has been some discussion about the attitude of the medical profession. I have had nothing from the American Medical Association but I have today received a telegram from the Medical Society of the State of New York saying:

> The chairman of the legislative committee of the Medical Society of the State of New York has instructed me to respectfully request your opposition to the bill, H. R. 3298, so long as it retains section (B).

Mr. LEONARD W. HALL. I think when we speak of the attitude of the American Medical Association and when we say they have not taken any action or expressed any attitude we mean at their meeting at Atlantic City where they met as a national body they did not take any action.

Mr. KEATING. They did not take any official action of which I am advised but I assume perhaps the gentleman has received a telegram similar to mine to the effect that the New York Medical Society is definitely in opposition to that section (B). Certainly I think that is one factor which we ought to take into consideration because presumably the medical society is trying to look out for the interests of the general public.

Mr. LEONARD W. HALL. I thank the gentleman.

The CHAIRMAN. The time of the gentleman from New York has expired.

Mr. HESELTON. Mr. Chairman, I move to strike out the last word.

Mr. Chairman, it is not pleasant for me to oppose an amendment proposed by my colleague and friend the gentle-

man from Minnesota [Mr. O'HARA] and supported by my other friends and colleagues from New York, Indiana, and Michigan. But I think it is incumbent upon some of the members of the committee who reported this bill out as a sound piece of legislation, to try at least to state the reasons why the pending amendment should not prevail. I suggest that the gentleman from California [Mr. HINSHAW] who spoke a few minutes ago, made a very sound, constructive suggestion to the membership here. As far as I am concerned, I do not see the dangers that others profess to see in this section of the bill.

In the first place, we have a precedent for it. It is entirely consistent with the act of 1938, when the Congress gave this administrator authority to list habit-forming derivative drugs named in section 502 (d). Incidentally, I do not think anyone would suggest that that authority has been abused.

In the second place, it has been repeatedly stated that if we adopt the amendment offered by the gentleman from Minnesota [Mr. O'HARA], and I do not think he will dispute this, that inevitably the situation will be left exactly where it is. It has been suggested that there is wider power. What is it? It is the power to prosecute criminally. It is the power to seize drugs. It is power to enjoin. I think everyone recognizes that there is both uncertainty and confusion in this picture; and certainly if that is so, a vote to adopt the amendment offered by the gentleman from Minnesota does nothing to remove that uncertainty and confusion.

I hope we will not forget that we removed from this bill in the consideration of it earlier—and I think it was wisely taken out—the part relating to efficacy. So we are dealing now only with the question of safety; safety for the American people who use these drugs. That is all there is in this.

If you are going back to the question of letting criminal procedures and seizures and injunctions determine it, you have 80 district courts in this country. You know and I know, with the jury system, it is utterly impossible to secure any consistency through that procedure. You will have one case decided one way and another decided in another way, and we would never have an end to it.

Moreover, there is the question of many involved in litigation. In one of the district courts recently there was a drug, a hormone case, which contributed to the growth of cancer. That was held in litigation for over 2 years. Meanwhile, irreparable damage was done to the people of this country who mistakenly used that drug.

I say it is a question of public welfare. It is a problem of public health. When the committee, by a majority of 19 to 4, after days of hearings, after almost a month of executive sessions, comes to the House with a recommendation such as this, I hope you will not lightly turn it aside, because action is needed.

Mr. O'HARA. Mr. Chairman, will the gentleman yield?

Mr. HILSELTON. I yield.

Mr. O'HARA. The gentleman refers to the drug which contributes to cancer. Does the gentleman admit that under this bill you have the same long drawn-out proceedings?

Mr. HESELTON. I doubt it.

Mr. O'HARA. Greatly magnified under this bill?

Mr. HESELTON. You know and I know that only a small fraction of the 30,000 mentioned in the list will be included in the list. In Canada they have a list with 18 drugs on it. With any degree of intelligent action we would have clear action in a reasonable time. Instead of projecting this over 30,000 cases, the gentleman from Texas [Mr. BECKWORTH] pointed out that in the hearings we had 140 cases between December 28, 1943, and April 1, 1951. I do want to do away with the tortuous case-by-case procedure. I do not want our people dragged into court and fined and given suspended sentences or imprisoned or enjoined or have their property seized because they do not know whether they are now safely selling drugs over the counter. They are justly entitled to all the certainty possible. I know the public that is using these drugs has some rights here today. I hope they will be recognized.

The CHAIRMAN. The time of the gentleman from Massachusetts has expired.

Mr. BECKWORTH. Mr. Chairman, I ask unanimous consent that all debate on this amendment and all amendments thereto close in 20 minutes.

The CHAIRMAN. Is there objection to the request of the gentleman from Texas?

Mr. AUGUST H. ANDRESEN. Mr. Chairman, I object.

Mr. BECKWORTH. Mr. Chairman, I move that all debate close in 20 minutes.

The CHAIRMAN. The question is on the motion.

The question was taken; and on a division (demanded by Mr. AUGUST H. ANDRESEN) there were—ayes 90, noes 19.

So the motion was agreed to.

The CHAIRMAN. The Chair has a list of names of the Members seeking recognition. The time will be divided equally between them and that will give each Member about 1½ minutes.

The gentleman from Wisconsin [Mr. KERSTEN] is recognized.

Mr. KERSTEN of Wisconsin. Mr. Chairman, as I understand the present bill, without the amendment it would be incumbent upon the Administrator to decide what drugs could be prescribed and those that could not be prescribed; in other words, he would have the responsibility of that rather very important function. It is true that there are a certain number of difficulties and there may be uncertainties in the present system, but in my humble opinion we are not solving them by putting this power in the hands of an administrator. I should like to make this short analogy: Suppose, for example, we were to put into the hands of an administrator the decision of what constituted the practice of medicine, in other words, an analogous field. Under the present system that question is determined by the courts, but if we were to put it into the hands of an administrator to determine what constituted the practice of medicine you would then be concentrating similar power in a Federal bureau. In my opinion a Federal administrator has not got the angelic mind he would have to have in order to do the things that the proponents of the present bill say he would have to do. In my opinion, with all of its difficulties the present system is superior. It is more in conformity with the facts, because you cannot take a considerable number of drugs and adopt a uniform rule for them. If a mistake is made by the Administrator the effects are Nation-wide.

The CHAIRMAN. The Chair recognizes the gentleman from Tennessee [Mr. EVINS].

Mr. EVINS. Mr. Chairman, on the whole, I think the committee has done a very good job insofar as two parts of this bill are concerned. However, I feel that the third section, section (B), is very controversial, and that it is neither necessary nor desirable. My objection to section (B) does not come about because I am representing any patent-medicine company or any special interests, as some may here have implied. I know of no drug-manufacturing company in my district.

My objection is based upon the additional authority to be here created and granted. There is already an existing body of law sufficient to take care of the situation. The public interest is already well served. There exists the Food and Drug Administration. We have the Food and Drug Administrator, a large body of laws, with authority to confiscate dangerous or deleterious drugs and to take them off the market. We have the Federal Trade Commission, which has authority to proceed against firms which may engage in unfair methods of competition or mislabeling, false advertising, or for making false and misleading statements, or engaging in misrepresentations. Adequate protection is thus afforded the public in this regard and no new authority is needed. I feel that there is a sufficient body of law at the present time, without giving additional authority to some administrator whereby a "black list" or "white list" of approved drug items might be set up. We might have a situation where the Administrator could say, "We will approve your product," and this approved product would be on the "white list," or the Administrator could say "I will not approve your drug for sale except by prescription," therefore this product would be on the "black list," as far as the sale over the counter is concerned. I do not think that situation should exist. Unless the O'Hara amendment is adopted, such a situation could develop.

It occurs to me that ample authority already exists both through the Federal Trade Commission and the Food and Drug Administration to cope with the situation concerning which section (B) of the bill is designed to afford protection. The authority proposed might well be properly administered. On the other hand, it could be misabused or abused.

I think existing authority is quite sufficient and that section (B) is not needed, and, therefore, that the O'Hara amendment should be adopted.

The CHAIRMAN. The Chair recognizes the gentleman from Idaho [Mr. WOOD].

Mr. BURDICK. Mr. Chairman, I ask unanimous consent that the time allotted me may be given to the gentleman from Idaho [Mr. WOOD].

The CHAIRMAN. Is there objection to the request of the gentleman from North Dakota?

There was no objection.

Mr. WOOD of Idaho. Mr. Chairman, several times the question has come up this afternoon as to why the American Medical Association has not appeared on one side or the other of this bill. I do not know why. I have not talked with that organization. I might point out that this is a drug bill, not doctor's bill. There is a National Association of Druggists, and, of course, they are the ones that should appear on a druggist's bill. I might also say that the experience of the American Medical Association with this particular Administrator has not been too happy in the past.

I have practiced medicine for 47 years. My opinion regarding this bill should be worth some attention.

How strange that medicine is the only one of the so-called learned professions about which every Tom, Dick, and Harry, and their wives, feel themselves perfectly competent to render expert opinions on almost every phase of that art and science.

Even more baneful is the fact that governmental bureaucrats also feel the urge to do something to help the lot of the supposed down-trodden and long-suffering public, writhing under so-called inadequate medical care, in spite of the fact that America is the Mecca of medical accomplishment, toward which the eyes of the world are turned, and also where medical care is more adequate than in any other country in the world.

This bill proposes to give a bureaucrat the authority to specify a list of so-called dangerous drugs and promulgate the rules under which they may be sold, or prescribed by physicians. Would you not feel that the physician through his national organization and its council on pharmacy and chemistry should be the authority to prepare such a list, and that the physicians themselves, through their national organization, should be the ones to prescribe the rules under which they may be used?

The Council on Pharmacy and Chemistry has investigated thousands of drugs in the past 40 or more years. They are the ones who have already gotten together such a list, and they have been sending that list to physicians for that length of time. Many of the States have followed the lead of this organization, and have promulgated lists of dangerous drugs to the pharmacists, and have forbidden their sale without a prescription.

And the law is working perfectly in the States where it is applied. If the druggist sells such drugs without a physician's orders, he is liable to the law for whatever trouble originates through such sale, and is directly liable to the State itself for the violation of the law. My experience with pharmacists in the past 47 years is that they are a group whose personal and professional standing is as high as that of any other profession. They are not potential lawbreakers.

Even in the States which do not yet possess this law, the remedy can be in the physician's hands, if he cares to use it. Long before Idaho passed the abovementioned law, it was my custom to write on the bottom of the prescription for one of these potentially dangerous drugs, the simple phrase: "Nonrepetatur," usually abbreviated to "Nonrep." A pharmacist is bound by all the rules of his profession not to refill that prescription, and I have never known or heard of a transgression of that rule.

As an illustration of how difficult it is to determine the correct answer to this problem, and how tragic it would be to have some ill-informed bureaucrat promulgate the rules for their use, as well as to tabulate the dangerous drugs, may be mentioned the fact that even a simple and harmless drug may be potent for harm under conditions which could only be determined by the physician in actual attendance on the patient. Even such simple things as salt, which could never be classed in that category, might shorten life in a case of dropsy, even in the amounts customarily used at the table.

Aspirin is not a dangerous drug, yet I cannot take even one tablet without vomiting. Penicillin is not generally classed as one of the more dangerous drugs, yet one of our most valued Republican Congressmen is in the hospital right now suffering from a severe allergy from even a small dose.

What then should be done with this bill? My own feeling is that it is about as useful as two thumbs on a hand would be. Pharmacists are already following the first section, and have been for years, and section 2 is impractical, or even foolish. Whatever is not useful and practical in legislation is harmful. Therefore, I feel it should be voted down.

I do feel, however, that the States which have not yet placed the dangerous drugs statute into effect should be urged to do so, through the force of public opinion, and through petitions sent to State legislatures by physicians' and pharmacists' National and State organizations.

The CHAIRMAN. The Chair recognizes the gentleman from Michigan [Mr. BENNETT].

Mr. WOLVERTON. Mr. Chairman, if the gentleman will yield, I ask unanimous consent that the time allotted to me be yielded to the gentleman from Michigan [Mr. BENNETT].

The CHAIRMAN. Is there objection to the request of the gentleman from New Jersey?

There was no objection.

Mr. BENNETT of Michigan. Mr. Chairman, the effect of the O'Hara amendment is relatively simple. What it does is to legalize the regulations under which the Food and Drug Administration has been operating in this field for a period of years. Section (B), as set forth in the O'Hara amendment, substantially embodies the terms of the present regulations. What is wrong with that, and why does the Food and Drug Administration want it changed? Simply this: Here is the procedure they are obligated to follow at present. If a drug manufacturer dispenses a prescription drug on a nonprescription basis, which Food and Drug feel is dangerous, they proceed against the manufacturer in several ways, either to prosecute him criminally, proceed against him by injunction, by enjoining him from further manufacture, or by confiscation, or by any combination of those remedies. Now what about the case of the druggist? Under this system if the retail druggist sells a drug in accordance with the label put on it by the manufacturer, if he acts in good faith, he is not subject to prosecution, even though the drug manufacturer would be. All they can do is to confiscate the drugs. If they confiscate his drugs, he has his recourse against the manufacturer. This is rational procedure.

But here is what the Administrator wants to do. He does not want to give the manufacturer or the druggist his day in court. The burden of proof is on the manufacturer or druggist. They must go into court and show that the drug is actually safe without a prescription. The Administrator wants an easier way. It is more difficult to give a man his day in court with the presumption in his favor than to proceed by administrative regulation, which provides no presumption for the citizen.

But it is safer and wiser to pursue a different course. Let us stay on the safe side by adopting this amendment.

The CHAIRMAN. The Chair recognizes the gentleman from Texas [Mr. ROGERS].

Mr. ROGERS of Texas. Mr. Chairman, I have listened with a great deal of interest to this heated debate, and I have concluded that the reference to the lobbies and the personalities and the bureaucratic control is something that we are not going to settle by passing this bill or adopting the O'Hara amendment. The focal point that should be considered that could remedy this entire situation is the substantial-evidence rule. The doctors do not have a great lobby that is against the American public. They are respectable people. So are the druggists, and certainly so are all of the Americans. But the one thing that they fear in this legislation is the fact that Oscar Ewing or John Doe or any other Administrator will have the power to set a rule or regulation, and that the man who is affected and hurt by that cannot go into court and have his day in court.

This Congress should go to work on correcting the ill that has been caused by the substantial-evidence rule, which has, in effect, taken away from the people of the United States their day in court and turned it over to administrative officials. When you rectify that situation, you are going to solve the problem that besets you because of bureaucratic control, and only then will it be solved.

The CHAIRMAN. The Chair recognizes the gentleman from Texas [Mr. BECKWORTH].

(Mr. CARLYLE asked and was given permission to yield the time allotted to him to Mr. BECKWORTH.)

Mr. BECKWORTH. Mr. Chairman, I was very much impressed by the statement of the gentleman from Nebraska [Mr. MILLER]. He emphasized that some 700 new drugs are coming on the market. Certainly this will add to the confusion that already exists. It is that confusion that this bill is designed to alleviate in part. When the inference is given that just two parts of this bill are important, and that this third part is not so important, that is just a misleading inference. This third part, the one that has been so controversial, is a very important part of this bill.

A lot has been said about a man's having his day in court. One of the things we are considering in this bill is that very question of the day in court, a day in court with reference to the sale of a given drug. The way the situation is today, you have your day in court after you have sold the drug, if you are a druggist, and if you are guilty you are already guilty. What we are trying to do in preventing the adoption of the O'Hara amendment is to see that a man has his day in court, as it were, before he is already guilty of something. If we adopt the O'Hara amendment, we shall continue to have the exact situation we have today, and added to this list that I have referred to on page 98 will be a lot of other druggists in this country who will be brought into proceedings after they have already performed the acts which subject them to the charge.

I cannot believe the members of this committee want to continue to cause a great segment of the businessmen of this country to have to undergo the uncertainty which has characterized their efforts.

The gentleman from Indiana [Mr. HALLECK] said that the Pure Food and Drug people say that the consumer is protected. Even though that be true, and I almost doubt it under the uncertainty that exists, still the druggist is one of the people we are proposing to try to protect, and he has stated in the most vocal manner he can through his national organization of some 34,000 that he does need that protection.

The CHAIRMAN. The Chair recognizes the gentleman from Michigan [Mr. CRAWFORD].

Mr. CRAWFORD. Mr. Chairman, it gives me pleasure to support the O'Hara amendment. Apparently I have some pretty good druggists in my district. I have never found any of them hanging on jail doors so far, and I do not know of any of them having been locked up—and I have been around some of the jails myself. I think the druggists are getting along pretty well. They do write me a great many times and say, "Please do not give any additional powers to the executive agencies of the Government." Therefore I am very delighted to have my friend, the gentleman from Minnesota, offer this amendment, and I hope it will be approved. Then I will have no objection to this bill as it has been presented, that is, if it can be amended in this way.

The CHAIRMAN. The Chair recognizes the gentleman from Ohio [Mr. CROSSER].

Mr. CROSSER. Mr. Chairman, and members of the Committee, I could not help but feel that if certain common words like "bureaucrat" and "socialist," and so on, were eliminated from the English language a lot of speeches could not have been made here today. The fact of the matter is that a lot of balderdash has been uttered in an effort to sabotage this bill. The thing that really counts is what the O'Hara amendment would take out of the bill. What protection has a man at this time? Yes, he can go ahead and defy the law and be tried and sent to jail. They say that the jails are not filled with people like that. But many of them have been sent to jail in just that way. This is the only way we can give a man a fair hearing before the man is in trouble and before an injunction has perhaps ruined his business and even his reputation. All this does is to undertake to put in the hands of this man the authority to do the job. I never knew much about this man but I saw no horns on him when he appeared before our committee. Perhaps we can get some sweet-looking fellow that would suit these people better. But I have seen nothing and heard nothing to indicate in the slightest degree any desire on his part to arrogate to himself any unlimited power. The fact of the matter is I thought the Administrator was unusually modest in not wanting to have a great deal of power put into his hands.

I hope that this abominable amendment may be voted down and the people of this country protected.

The CHAIRMAN. The time of the gentleman from Ohio [Mr. CROSSER] has expired.

All time has expired.

The question is on the amendment offered by the gentleman from Minnesota [Mr. O'HARA].

The question was taken; and on a division (demanded by Mr. HARRIS) there were—ayes 141, noes 85.

So the amendment was agreed to.

The CHAIRMAN. The question is on the committee amendment as amended.

The committee amendment as amended was agreed to.

The CHAIRMAN. Under the rule, the Committee will rise.

Accordingly the Committee rose; and the Speaker having resumed the chair, Mr. COLMER, Chairman of the Committee of the Whole House on the State of the Union, reported that that Committee, having had under consideration the bill (H. R. 3298) pursuant to House Resolution 354, he reported the same back to the House with an amendment adopted in Committee of the Whole.

The SPEAKER. Under the rule, the previous question is ordered.

The question is on agreeing to the committee amendment.

The committee amendment was agreed to.

The SPEAKER. The question is on the engrossment and third reading of the bill.

The bill was ordered to be engrossed and read a third time, and was read the third time.

The SPEAKER. The question is on the passage of the bill.

The bill was passed.

A motion to reconsider was laid on the table.

MESSAGE FROM THE SENATE

A message from the Senate, by Mr. Carrell, one of its clerks, announced that the Senate had passed without amendment a joint resolution of the House of the following title:

H. J. Res. 303. Joint resolution to provide housing relief in the Missouri-Kansas-Oklahoma flood disaster emergency.

The message also announced that the Senate agrees to the report of the committee of conference on the disagreeing votes of the two Houses on the amendments of the Senate to the bill (H. R. 4329) entitled "An act making appropriations for the government of the District of Columbia and other activities chargeable in whole or in part against the revenues of such District for the fiscal year ending June 30, 1952, and for other purposes."

RESIGNATIONS FROM COMMITTEES

The SPEAKER laid before the House the following resignation which was read by the Clerk:

HOUSE OF REPRESENTATIVES,
Washington D. C., July 27, 1951.
Hon. SAM RAYBURN, *Speaker,*
House of Representatives,
Washington, D. C.

DEAR MR. SPEAKER: I herewith submit my resignation to the House Committee on Interstate and Foreign Commerce effective July 30.

Respectfully,

WILSON D. GILLETTE.

The SPEAKER. Without objection the resignation is accepted.

There was no objection.

The SPEAKER laid before the House the following resignation which was read by the Clerk:

HOUSE OF REPRESENTATIVES,
Washington, D. C., August 1, 1951.
Hon. SAM RAYBURN,
Speaker of the House,
United States Capitol,
Washington, D. C.

DEAR SIR: I hereby tender my resignation as a member of the Committee on Veterans' Affairs effective this date.

Yours very truly,

HARMAR D. DENNY, JR.

The SPEAKER. Without objection the resignation is accepted.

There was no objection.

ELECTION TO COMMITTEE

Mr. MARTIN of Massachusetts. Mr. Speaker, I offer a privileged resolution (H. Res. 365).

The Clerk read as follows:

Resolved, that HARMAR D. DENNY, JR., of Pennsylvania be, and he is hereby, elected to the Committee on Interstate and Foreign Commerce of the House of Representatives.

The resolution was agreed to.

82D CONGRESS } HOUSE OF REPRESENTATIVES { REPORT
1st Session } { No. 700

AMENDING SECTION 503 (b) OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT

JULY 16, 1951.—Committed to the Committee of the Whole House on the State of the Union and ordered to be printed

Mr. WILLIAMS of Mississippi, from the Committee on Interstate and Foreign Commerce, submitted the following

REPORT

[To accompany H. R. 3298]

The Committee on Interstate and Foreign Commerce, to whom was referred the bill (H. R. 3298) to amend section 503 (b) of the Federal Food, Drug, and Cosmetic Act, having considered the same, report favorably thereon with an amendment and recommend that the bill as amended do pass.

The amendment is as follows:

Strike out all after the enacting clause and insert the following:

That subsection (b) of section 503 of the Federal Food, Drug, and Cosmetic Act, as amended, is amended to read as follows:

"(b) (1) A drug intended for use by man which—

"(A) is a habit-forming drug to which section 502 (d) applies; or

"(B) because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, has been determined by the Administrator, on the basis of opinions generally held among experts qualified by scientific training and experience to evaluate the safety and efficacy of such drug (and, where a public hearing is required by paragraph (5), on the basis of evidence adduced at such hearing by such experts), to be safe and efficacious for use only after professional diagnosis by, or under the supervision of, a practitioner licensed by law to administer such drug; or

"(C) is limited by an effective application under section 505 to use under the professional supervision of a practitioner licensed by law to administer such drug,

shall be dispensed only (i) upon a written prescription of a practitioner licensed by law to administer such drug, or (ii) upon an oral prescription of such practitioner which is reduced promptly to writing and filed by the pharmacist, or (iii) by refilling any such written or oral prescription if such refilling is authorized by the prescriber either in the original prescription or by oral order which is reduced promptly to writing and filed by the pharmacist. The act of dispensing a drug contrary to the provisions of this paragraph shall be deemed to be an act which results in the drug being misbranded while held for sale.

"(2) Any drug dispensed by filling or refilling a written or oral prescription of a practitioner licensed by law to administer such drug shall be exempt from the

EXHIBIT A

requirements of section 502, except paragraphs (a), (i) (2) and (3), (k), and (l), and the packaging requirements of paragraphs (g) and (h), if the drug bears a label containing the name and address of the dispenser, the serial number and date of the prescription or of its filling, the name of the prescriber, and, if stated in the prescription, the name of the patient, and the directions for use and cautionary statements, if any, contained in such prescription. This exemption shall not apply to any drug dispensed in the course of the conduct of a business of dispensing drugs pursuant to diagnosis by mail or otherwise without examination of the patient or to a drug dispensed in violation of paragraph (1) of this subsection.

"(3) The Administrator may by regulation remove drugs subject to section 502 (d) and section 505 from the requirements of paragraph (1) of this subsection when such requirements are not necessary for the protection of the public health.

"(4) A drug which is subject to paragraph (1) of this subsection shall be deemed to be misbranded if at any time prior to dispensing its label fails to bear the statement 'Caution: Federal law prohibits dispensing without prescription'. A drug to which paragraph (1) of this subsection does not apply shall be deemed to be misbranded if at any time prior to dispensing its label bears the caution statement quoted in the preceding sentence or any other statement which represents or implies that the dispensing of the drug without the prescription of a licensed practitioner is prohibited.

"(5) Any interested person may file with the Administrator a petition proposing the making of a determination, or the modification of a determination made or proposed to be made, by the Administrator pursuant to subparagraph (B) of paragraph (1). The filing of a petition for the purpose of opposing a proposed determination that a drug is one to which such subparagraph (B) applies shall stay the operation of paragraph (1) with respect to such drug until a petition for judicial review can be filed and interim relief sought under section 10 (d) of the Administrative Procedure Act. The petition shall set forth in general terms the proposal contained therein, and shall state reasonable grounds therefor. The Administrator shall give public notice of the proposal made in the petition and shall give to all interested persons a reasonable opportunity to present their views thereon, orally or in writing, and as soon as practicable thereafter shall make public his action on the proposal. At any time prior to the thirtieth day after such action is made public, any interested person may file with the Administrator objections to such action, specifying with particularity the changes proposed, stating reasonable grounds therefor, and requesting a public hearing for the taking of evidence of experts who are qualified by scientific training and experience to testify on the question of whether the drug in question is safe and efficacious for use only after professional diagnosis by, or under the supervision of, a practitioner licensed by law to administer such drug. The Administrator shall thereupon, after appropriate notice, hold such public hearing. As soon as practicable after the hearing, the Administrator shall make his determination and issue an appropriate order. The Administrator shall make his order only after a review of the whole record and in accordance with the reliable, probative, and substantial evidence, and shall make detailed findings of the facts on which he based his order. Such order shall be subject to judicial review in accordance with the provisions of section 701 (f) and (g).

"(6) Nothing in this subsection shall be construed to relieve any person from any requirement prescribed by or under authority of law with respect to drugs now included or which may hereafter be included within the classifications stated in section 3220 of the Internal Revenue Code (26 U. S. C. 3220), or to marihuana as defined in section 3238 (b) of the Internal Revenue Code (26 U. S. C. 3238 (b))."

SEC. 2. The provisions of this Act shall take effect six months after the date of its enactment.

WHAT THE BILL DOES

This bill amends the Federal Food, Drug, and Cosmetic Act to accomplish two broad objectives:

(1) To strengthen the protection of the public health against dangerous abuses in the sale of potent prescription drugs;

(2) To relieve retail druggists and the public from burdensome and unnecessary restrictions on the dispensing of drugs which may be safely used without supervision by a physician.

The bill does this by placing in the Federal Food, Drug, and Cosmetic Act express provisions which will eliminate confusion and dissatisfaction which exist under the present rather general provisions dealing with the labeling and dispensing of drugs which may be sold only on prescription and drugs which may be sold over the counter.

The bill, as amended, is designed to solve these labeling and dispensing problems in the following ways:

1. By providing for a clear-cut method of distinguishing between "prescription" drugs (that is, drugs which are not suitable for self-medication because they should be used only under the supervision of a physician, and which therefore should be dispensed only on prescription) and "over-the-counter" drugs (that is, drugs which are suitable for self-medication, and which therefore should be permitted to be dispensed freely "over-the-counter"), and by requiring that drugs be so labeled as to indicate to the retail druggist and to the general public into which of these two classes they fall.

Under the present law, and the regulations issued thereunder, the initial responsibility is upon the manufacturer to decide whether his drug is unsuitable for self-medication and therefore must be labeled with a caution legend (that is, a warning that the drug in question may be dispensed only by or on prescription of a physician) and may be sold only on prescription, or whether his drug is suitable for self-medication and therefore must be labeled with adequate directions for use and may be sold freely over the counter. Lack of uniformity among manufacturers in interpreting the present law and regulations has led to great confusion in the labeling of drugs for prescription sale and for over-the-counter sale.

2. By expressly setting forth in the statute the restrictions applicable to the dispensing of "prescription" drugs.

At present the restrictions on dispensing "prescription" drugs are not specifically stated in the statute. As hereafter explained, they result from conditions which have been imposed by the Federal Security Administrator in connection with certain exemptions which he is authorized to grant under the present law.

3. By authorizing the filling and refilling of telephone prescriptions under appropriate safeguards.

The present law recognizes written and signed prescriptions only, in complete disregard of the need for the use of the telephone in prescribing medicines.

4. By specifying in detail the conditions under which pharmacists may refill prescriptions.

Under the present law no prescription may be lawfully refilled unless refilling is specifically authorized in writing by the prescribing physician. This makes it unlawful for the pharmacist to refill prescriptions without written authorization even for drugs which are suitable for self-medication. The bill would permit the refilling of prescriptions for such drugs without authorization from the physician. However, in the case of dangerous drugs, habit-forming drugs, and new drugs which are limited to use under medical supervision, it would prohibit refilling unless the prescribing physician specifically authorizes the refill.

Committee Hearings

The committee held extensive hearings on this bill. The testimony amply supports the conclusion that legislation is urgently needed and it is believed that the provisions of the bill, as amended, will further the protection of the public health by meeting the complex problems which were brought to the committee's attention in the hearings.

The committee has received communications with respect to this proposed legislation from the Federal Security Administrator, the Deputy Attorney General, and the Administrative Office of the United States Courts. These communications are printed in an appendix to this report.

General Statement

Prescription drugs.—There is urgent need for affirmative and clear provisions in the law to deal with the labeling of prescription drugs and the restrictions upon their sale.

The present law prohibits the over-the-counter sale of drugs labeled as being for prescription sale only, but it does this in the following indirect manner.

A drug is required by present law to bear "adequate directions for use." This requirement may be relaxed by regulations of the Federal Security Administrator when such directions are not necessary for the protection of the public health. Drugs suitable for use only by or under the direction of a licensed practitioner have been exempted from the adequate directions requirement on condition that they be labeled "Caution—To be dispensed only by or on prescription of a physician." If a druggist sells without a prescription a drug bearing this caution label, the drug is misbranded and the druggist violates the act.

The present law and regulations do not provide a satisfactory method for determining the drugs which properly fall within the prescription class. Furthermore, these matters should be regulated by specific statutory provisions rather than, as at present, largely through administrative regulations.

Under the present regulation the retail druggist is often unable to know, until the question is settled by litigation, whether a particular drug can be sold on prescription only. The regulation requires the prescription legend on drugs which are generally regarded as safe and efficacious for use only under medical supervision. All other drugs are required to bear adequate directions for use, and this means directions adequate for a layman to follow. The initial responsibility is upon the manufacturer to decide whether his drug belongs in one class or the other.

If a manufacturer decides that his drug is suitable for use only under medical supervision, and labels it with the prescription legend, it is necessary, if the Administrator disagrees on the basis of expert advice to that effect, to bring a criminal prosecution, a seizure action, or an injunction to require that the legend be taken off and adequate directions for use written. On the other hand, if the manufacturer decides that his drug is suitable for use by a layman without consulting a physician, and labels it with directions for use, but the Administrator disagrees on the basis of expert advice to that effect, an action must be

brought charging that the drug violates either section 502 (a) by being represented falsely to be safe and effective for lay use or section 502 (j) because the drug may be dangerous to health when used as directed. Litigation, at best, is a slow process and can be directed at only one party and one product at a time. It is not a satisfactory method for establishing correct future labeling of a particular drug regardless of who manufactures it.

The practical effect of the present regulatory system has been great confusion in the use of the prescription legend. Many products of identical composition, placed on the market by different manufacturers, were shown to the committee in a practical demonstration of the druggists' dilemma. One would bear the prescription legend while another of the same composition would provide directions for use.

For example, a sample of precipitated chalk manufactured by one manufacturer was labeled with the legend:

Caution: To be dispensed only by or on the prescription of a physician, dentist, or veterinarian, or otherwise used only for manufacturing purposes. This restriction applies only to medicinal uses.

Another sample of the same drug manufactured by a different manufacturer carried the following directions for use:

Antacid—Average dose: one-quarter teaspoonful in water. May also be used as a tooth powder.

Another example involved strychnine sulfate in small doses (one-sixtieth grain). This drug manufactured by one manufacturer carried the legend:

Caution: To be dispensed only by or on the prescription of a physician.

The same drug manufactured by another manufacturer carried the following directions for use:

To improve appetite and digestion. For adults only: 1 tablet before meals. Other doses as prescribed by physician. Warning: Do not take more than 6 tablets in 24 hours.

A third example involved dehydrocholic acid. This drug manufactured by one manufacturer carried the caution legend:

To be used only by or on the prescription of the physician.

The identical drug produced by another manufacturer carried the following directions for use:

Dosage: *Adults*—1 tablet 3 times daily with or after meals. *Children*—Only under the direct supervision of a physician.
In the presence of jaundice, this product should be used only under the direction of a physician.

It should be noted that these directions for use do not state the condition for the treatment of which this particular drug is to be used.

Also presented were samples of acetophenetidin and acetophenetidin with salol which, as manufactured by one manufacturer, carried the caution legend, and as manufactured by another manufacturer carried directions for use.

Some products were shown to the committee which had something like the prescription legend and also recommended dosages. The druggist would not even know, in such a case, the class in which the manufacturer intended to place such drugs.

For example, in the case of ammonium chloride (7½ grains), one manufacturer labeled this drug with a caution legend:

Caution: To be dispensed only by or on the prescription of a physician.

The same drug manufactured by another manufacturer carried the following legend:

Adult dose—one or two tablets repeated as directed by the physician.

A second sample involved thyroid tablets. One manufacturer labeled this drug:

Caution: To be dispensed by or on the prescription of a physician. Indiscriminate use may be harmful.

Another manufacturer labeled the identical drug as follows:

Directions: To be used on advice or prescription of a physician.

It should be noted that while the "directions" refer to prescription of a physician, confusion is caused to the druggist by failing to use the standard caution legend prescribed by the regulations.

A third example involves quinidine sulfate. One manufacturer labeled this drug with the standard caution legend:

Caution: To be dispensed only by or on the prescription of a physician.

Another manufacturer labeled the same product with the following legend:

Adult dose—1 tablet as directed by the physician.

An example of three different labels for the same drug was also presented. Methenamine was labeled by the first manufacturer:

Adult dose—1 to 3 tablets as directed by the physician.

The second manufacturer labeled this product:

Caution: To be used only by or on the prescription of a physician.

The third manufacturer labeled this drug with the following directions for use:

Dose: As a urinary antiseptic, 1 tablet with a large glass of water twice a day for not longer than 7 days. Urine should be kept acid. Other dosage or uses as directed by physician.

The confusion existing under present law has resulted in inadequate protection of the public health. In a situation where the druggist is uncertain as to the drugs which may be dispensed only on prescription, it is inevitable that there have been many cases of indiscriminate and unauthorized over-the-counter sales of dangerous drugs and other drugs which should be used only under medical supervision.

The committee believes that the present public health problem in connection with the unlawful labeling and dispensing of prescription drugs exists largely because the present law is not clearly and affirmatively expressed in the statute. The overwhelming majority of drug manufacturers and pharmacists are anxious to comply with provisions of law which they can understand. In contrast with the present law, this proposed legislation will be clear and readily understood. It is believed that after this legislation is enacted the need for enforcement, through criminal action, seizure, and injunction, will arise only in the cases of a few violators who are oblivious to their obligations to society.

Under the bill, as amended, three types of drugs will be limited to prescription sale, namely, habit-forming drugs, "dangerous" drugs,

and new drugs which, under the present law, already may be limited to use under professional supervision. The confusion under present law exists primarily with respect to "dangerous" drugs, that is, those not suitable for self-medication. The bill provides a workable method by which clear determinations can be made, at the earliest practicable time, as to whether particular drugs are "dangerous" drugs. Such determinations will be made by the Federal Security Administrator on the basis of a statutory standard, and a list of such drugs will be formulated. The Administrator's determinations will be subject to judicial review.

All drugs which, by the amended bill, are restricted to prescription sale *must* carry the prescription legend: "Caution—Federal law prohibits dispensing without prescription." No other drugs will be permitted to carry this prescription label. The latter drugs, as required by the present law, must carry adequate directions for use telling the [illegible] what the drug is for and how it is to be used.

The bill, as amended, expressly provides that the drugs limited to prescription sale (when intended for human consumption) shall be dispensed only upon a written or oral prescription of a licensed practitioner. Oral prescriptions will be permissible only when promptly reduced to writing by the pharmacist and filed by him. Refilling of prescriptions will be permissible only if authorized in the original prescription or by an oral order of the licensed practitioner which is promptly reduced to writing by the pharmacist and filed by him.

This legislation will provide for certainty which is lacking under the present law and which is very important to the enforcement agency, to the retail druggist, and to the public. The committee believes that these changes in the law will impose no hardship on the reputable manufacturer and will, indeed, afford him a means of knowing, before he subjects his products to seizure and himself to prosecution, whether his drug must be labeled for prescription dispensing or for over-the-counter sale.

Certainty is important to the enforcement agency because it permits more effective enforcement through appropriate control over drugs that are too dangerous, or otherwise unsuitable, to be used by a layman without medical diagnosis or supervision. Under this proposed legislation it will be possible to *prevent* injury to the public, as contrasted with the present system which is largely concerned with punishing past violations.

Oral prescriptions.—Another phase of the present law which needs modification and clarification is with respect to the filling and refilling of oral, or telephone, prescriptions. The present law does not recognize the practice of dispensing drugs on oral prescription. For the convenience of the public, the retail druggist, and the physician, the committee feels that the filling and refilling of prescriptions on oral order, under proper safeguards, should be permitted. The bill, as amended, contains appropriate provisions, explained below in this report, which deal with this question.

Refilling prescriptions.—The Food and Drug Administration has found that a serious public-health problem exists in the indiscriminate refilling of prescriptions for dangerous and habit-forming drugs. Examples were cited in which death resulted from unauthorized refillings of prescriptions for barbiturates and benzedrine. A 45-year-old man, father of two children, was found dead in 1950 from an overdose of barbiturates obtained on a prescription written in 1945

or 1946. Investigation revealed that the original prescription had been refilled many times without consulting the prescribing physician. The man became addicted to this habit-forming drug and shortly before his death was taking many times the therapeutic dose to satisfy his cravings. His death would not have occurred had the physician's instructions been followed.

The benzedrine death occurred in 1950, 13 years after the original prescription was written. The widow stated that the prescription had been repeatedly refilled during that time. The physician had last seen the deceased in 1937 and at that time had written a prescription for 14 10-milligram tablets. The amount dispensed in the refills had substantially increased until just before his death this man was taking as much as 25 tablets a day. The prescribing physician stated that he had not intended that the patient take more than the original 14 tablets which he prescribed.

The Food and Drug Administration has interpreted the existing law to prohibit the unauthorized refilling of prescriptions for all drugs. This interpretation, which is doubtless justified by the terms of the present law, is needlessly restrictive in making illegal the refilling of prescriptions for those drugs that can be bought over the counter without prescriptions. Furthermore, it is difficult for the enforcement official to meet the refill problem as it relates to dangerous and habit-forming drugs when that matter is not expressly dealt with in the statute.

The committee has included in the bill, as amended, express provisions, explained below in this report, to clarify the present law with respect to the refilling of prescriptions.

Determination of What Drugs Are Prescription Drugs

CONFLICTING LEGISLATIVE RECOMMENDATIONS

The committee was confronted with a dilemma in that the trade and professional organizations representing the different interested groups have made conflicting recommendations. The National Association of Retail Druggists, on the one hand, has urged that in the interest of achieving the greatest possible certainty for the retail druggists and the general public, the Federal Security Administrator should be vested with the power to determine on the basis of a statutory standard, but subject to judicial review, which drugs are to be sold on prescription only. The drug manufacturers, on the other hand, represented by the American Pharmaceutical Manufacturers' Association, the American Drug Manufacturers' Association, and the Proprietary Association, and those pharmacists who are represented by the American Pharmaceutical Association, have opposed the vesting of any such authority in a Federal official. They have contended that the determination of which drugs may be sold only on prescription should be left to judicial determination, on the basis of a statutory standard, in court proceedings (seizure, criminal prosecution, or injunction) instituted by the Federal enforcement officials.

THE COMMITTEE'S DECISION

The committee has thoroughly studied the arguments adduced by both sides in favor of their respective proposals. It has come to the conclusion that administrative determination, subject to judicial

review, gives the greatest promise of effectively relieving the retail druggists and the general public from the presently existing confusion. This decision has been made somewhat reluctantly because the committee is deeply conscious of the fact that the power to determine which drugs are prescription drugs and which are over-the-counter drugs is one which affects drug manufacturers, drug wholesalers, retail druggists, pharmacists, physicians, and, last but not least, the general public. The reasons for the committee's decision are set forth below.

PROPOSED STATUTORY LIST

The committee studied the question of whether such a grant of power to an administrative officer could be avoided by inserting in the bill a list of drugs that may be sold on prescription only. The committee, however, has come to the conclusion that such a list could be formulated only after extensive hearings involving expert testimony with respect to each drug that might be placed on this list. Furthermore, over the years, a statutory list of prescription drugs would prove too inflexible to keep pace with the rapid changes and developments occurring in the drug field.

CASE-BY-CASE JUDICIAL DETERMINATION

The committee gave careful consideration to the proposal of the drug manufacturers that the determination of which drugs may be sold only on prescription should be left solely to judicial determination in seizure, injunction, and criminal cases.

Testimony was presented that this case-by-case method of judicial determination would unnecessarily and unfairly involve retail druggists in court proceedings. This would come about, so the retail druggists argue, because the Federal Security Administrator would continue to have the power, which he now has and which he now exercises, to seize drugs on the shelves of retail druggists (or to institute injunction or criminal proceedings against druggists) primarily for the purpose of bringing test cases to determine whether the drugs in question are prescription drugs or over-the-counter drugs. Not infrequently, unfavorable publicity results from such seizures or court proceedings to the great damage of the druggist, injuring him not only financially but also lowering his standing in the community.

The committee feels that the institution of test cases to determine for the future whether a given drug may be sold only on prescription or may be sold over the counter does not constitute a desirable and effective use of the judicial process. Actually, in such cases, the Government would not be seeking primarily the decision of the court that a particular person had violated the law. It would be seeking a determination of the court that drug "A," for example, is too dangerous for self-medication, and that, therefore, in the future, it should be sold only on prescription, or conversely, that drug "B" which was labeled with the prescription legend, and which failed to set forth on its label proper directions for use, was actually a safe drug which could be sold over the counter.

CONSIDERATIONS WHICH INFLUENCED THE COMMITTEE'S DECISION

The considerations which have influenced the committee in its decision to provide for administrative determination subject to judicial review may be summarized as follows:

First. The administrative process will involve as parties only those primarily interested, namely, the drug manufacturers. It would not involve the retail druggists, whose interest is limited to securing certainty as to how they may sell a given drug.

Second. The task of determining which drugs shall be sold only on prescription is, in its nature, essentially a legislative or rule-making function, unsuited for solution solely through the judicial process.

Third. The committee's decision is entirely consistent with the one made in 1938 when Congress gave the Administrator the authority to list habit-forming derivatives of the drugs named in section 502 (d), and it has not been suggested that that authority has been abused.

Fourth. In the opinion of the committee the judicial-review provisions afford adequate protection against arbitrary or legally unjustified action on the part of the Administrator. This particular phase is discussed below in greater detail under the heading "Judicial review."

Fifth. If the proposal of the drug manufacturers were adopted, great confusion might result from conflicting court decisions with respect to the same drug in different jurisdictions. One United States district court might hold that a given drug was dangerous, judged by the statutory standard, while another district court might hold the opposite. There are more than 80 United States district courts. Even if all of the cases were tried without juries, it would be almost beyond the realm of possibility that uniformity could be obtained. With the vagaries of the jury system, it is believed that uniformity of decisions would be wholly impossible. One firm might obtain a judgment favorable to it that a particular drug was safe for over-the-counter sale, while others in the industry were required to limit it to prescription sale.

From a public-health standpoint, the users of drugs should not be subjected to the hazards of delay incident to litigation. A recent hormone case, decided in favor of the Government by the United States Court of Appeals for the Ninth Circuit, took more than 2 years in litigation in order to limit the drug to prescription use under existing law. The drug was capable of causing accelerated growth of cancer of the prostate, a condition not uncommon in the fifties and sixties. While the litigation was in progress irreparable injury was done. Under the suggestion to use the case-by-case method of judicial determination, the druggist, on whom the burden of prosecution would fall most directly, would be in a very difficult position. He would have to determine at his risk whether a drug which the manufacturer had labeled with directions for use for over-the-counter sale had been correctly classified. He would follow the label only at his peril.

Finally, it is difficult to understand why the drug manufacturers themselves should prefer to have their products seized or to be proceeded against in criminal cases merely toward the end of securing a determination as to whether a particular drug is or is not a prescription drug.

LIMITATIONS ON ADMINISTRATOR'S POWERS

The committee recognizes that the Federal Security Administrator is not, and should not be expected to be, an expert qualified to decide which drugs should be sold on prescription only and which should be sold freely over the counter. Therefore, in the bill, as amended, the committee has provided that the Administrator is to make this determination on the basis of a statutory standard. The standard which he is to apply is essentially the same standard presently contained in the regulations of the Federal Security Administrator promulgated under section 502 (f) of the Federal Food, Drug, and Cosmetic Act. That standard has been accepted by the drug trade as proper and adequate, and representatives of drug manufacturers, appearing before the committee, urged that it be written into the law as the basis for case-by-case judicial determinations.

Under this standard a drug will be adjudged a prescription drug if because of its toxicity or any other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, it is unsafe or inefficacious for use without professional supervision. In applying this standard to a given drug, the Administrator is directed to follow the opinions generally held among experts qualified by scientific training and experience to evaluate the safety and efficacy of the drug in question. If any interested party desires a public hearing on whether a particular determination by the Administrator on that basis is justified, he may demand such a hearing. At the hearing the evidence taken will be evidence presented by qualified experts. The Administrator must base his action, after the hearing, on the testimony given by such experts, not on his own personal views. In short, the committee amendment, in effect, places the Federal Security Administrator in the role of collecting informed medical opinions and, in either placing the drug on the prescription list or deciding that the drug is suitable for over-the-counter sale, he merely reflects the opinions generally held among medical experts.

By incorporating this standard in the law and by specifying the process to be used by the Administrator in applying it, the committee believes it has achieved a practical and equitable solution of the dilemma in which it found itself as a result of the conflicting legislative recommendations submitted by the trade and professional organizations in the drug field.

EFFICACY OF DRUGS

The standard which the bill, as amended, would write into the law (subparagraph (B) of paragraph (b) (1) of the amendment) contains the words "efficacy" and "efficacious." The use of these words has given rise to some apprehension, particularly on the part of manufacturers of proprietary drugs (patent medicines), that the Federal Security Administrator might have the power to determine which drugs are "efficacious" or "effective" and which are not. It may be stated unequivocally that this provision is not intended to grant any such power to the Administrator, nor does it lend itself in any way to such an interpretation.

The provision provides for a determination by the Administrator whether a given drug—

on the basis of opinions generally held among experts qualified by scientific experience to evaluate the safety and *efficacy* of such drugs * * * [is] * * * safe and *efficacious for use only after professional diagnosis by, or under the supervision of, a practitioner licensed by law to administer such drug;* * * *.

The question to be determined by the Administrator on the basis of expert opinion, therefore, is not whether a drug is efficacious but whether it can be used efficaciously without professional diagnosis or supervision.

The provision assumes that the drug is effective in the hands of a physician, and the reason for putting it on the prescription list is that it is only effective when used under professional supervision.

For example, no qualified person questions the efficacy of quinidine sulfate in the treatment of certain heart diseases. However, in view of the serious nature of the disease and the necessity of adjusting the dose to the individual patient's need, the drug obviously cannot be used with efficacy except when used under professional supervision. While the drug is not dangerously toxic, the user may nevertheless die if in the course of self-medication he should fail to take a dose which is suited to his individual needs.

JUDICIAL REVIEW

A determination by the Administrator, though based on expert testimony, will be reviewable by the courts. By making applicable the provisions of section 701 (f) and (g) of present law, the amended bill will insure that any interested person may obtain judicial review by a United States court of appeals and, upon certiorari, by the Supreme Court of the United States.

The reviewing court will have power to set aside the Administrator's order if it is not in accordance with law, and the Administrator's findings as to the facts will be conclusive only if supported by reliable, probative, and substantial evidence on the record considered as a whole.

The bill, as introduced, proposed to permit any interested person dissatisfied with a determination of the Administrator to secure judicial review in the nature of a trial de novo in a court of appeals of the United States. This provision was intended to give to an aggrieved party the greatest possible insurance of fairness and justice. However, the committee is convinced that no matter how well intended, this proposal was impractical.

The committee came to this conclusion largely on the basis of the very earnest presentation made by the Honorable Harold M. Stephens, Chief Judge of the United States Court of Appeals for the District of Columbia Circuit, speaking on behalf of, and by direction of, the Judicial Conference of the United States. The gist of Judge Stephens' testimony was that the needs of the United States courts demand that the judicial review of administrative determinations be limited to a review of whether the administrative determination is based on reliable, probative, and substantial evidence considering the whole record made before the administrative agency. This is the extent and character of review provided for under the provisions of the Administrative Procedure Act, enacted in 1946.

It was pointed out by Judge Stephens that the United States courts of appeals are appellate courts and not trial courts, and that such courts for several reasons are not equipped to handle trials. First, the United States courts of appeals are three-judge courts. It has been the experience of the United States courts that trials are conducted more efficiently by single judges than by three or more judges. Questions involving the admissibility of evidence, for example, have to be determined frequently and promptly in the course of a trial. While a single judge can rule on these questions as they occur without delay, three judges would have to confer on each issue as it was raised and such conferences involve necessarily delay, thus making the trial a cumbersome affair. Furthermore, United States courts of appeals, being appellate courts rather than trial courts, do not have jury boxes in their courtrooms, do not have jury lists, and do not have jury rooms. All of these considerations militate against providing for de novo trials in United States courts of appeals.

If, on the other hand, the district courts of the United States were to be required to determine the validity of administrative determinations in all instances on the basis of de novo trials, such a great additional burden would be placed upon these courts that the number of Federal district court judges would have to be greatly increased.

Furthermore, Judge Stephens pointed out with great emphasis that recent decisions of the Supreme Court of the United States (*Universal Camera Corp.* v. *N. L. R. B.* and *Labor Board* v. *Pittsburgh S. S. Co.*, decided February 26, 1951) insure that the ordinary and usual type of judicial review of administrative action (which is the type provided for by this bill, as amended, and by the Administrative Procedure Act) affords full protection against arbitrary or legally unjustified action by administrative officials.

In addition to the foregoing objections to the proposal to provide for judicial review in a trial de novo, it is believed that the proposal might be unconstitutional on the ground that it would seek to have Federal "constitutional" courts exercise a function which is essentially legislative or administrative, rather than judicial. This point is discussed in the letters from the Deputy Attorney General and the Federal Security Administrator printed in the appendix to this report.

Oral Prescriptions

The bill, as amended, contains provisions which give statutory recognition to the frequent practice engaged in by physicians of using the telephone to transmit prescriptions to a pharmacist. The use of the telephone in prescribing medicines is of great convenience to the users of such medicines and is, in some areas of this country, essential to the public health. The statutory recognition of oral prescriptions proposed by the bill does away with the unrealistic provisions of the present Federal Food, Drug, and Cosmetic Act which recognizes a written and signed prescription only. The committee amendment would permit the use of oral prescriptions in the case of all drugs. However, in case of habit-forming drugs, dangerous drugs, or new drugs which are limited to prescriptions, an oral prescription would have to be reduced promptly to writing and filed by the pharmacist.

The committee gave serious consideration to whether it was desirable to place additional safeguards on oral prescriptions. However, it was determined that the admittedly limited safeguards provided for in the committee amendment would be adequate until the need for more rigid requirements has been proven by experience.

If the committee amendment is enacted into law, it is hoped that the Commissioner of Food and Drugs will observe closely the effect of the provisions with respect to oral prescriptions and will report to the responsible committees of both Houses any abuses that might develop as a consequence of the relaxation of the written prescription requirement now contained in the Federal Food, Drug, and Cosmetic Act.

Refilling Prescriptions

The bill, as amended, deals expressly with the troublesome problem of refilling prescriptions. Under the present law a drug dispensed on a "written prescription, signed by a physician," is entitled to certain limited exemptions from the labeling requirements that ordinarily apply to drugs. Through the force of these exemptions, drugs sold on written prescriptions are not misbranded even though they fail to meet the labeling requirements of the act. The Food and Drug Administration, relying upon its understanding of what is meant by a "written prescription," has taken the position that a drug dispensed by refilling a prescription without the knowledge or consent of the prescriber is not dispensed on prescription and thus is not exempt from the labeling provisions of the act. Without such exemption, the drug is misbranded by dispensing it without the prescriber's authorization.

This administrative position meets the public health problems found to exist by reason of the indiscriminate and unauthorized refilling of prescriptions for dangerous drugs and for other drugs that require medical supervision for their effective use. Some drugs, such as amphetamine (benzedrine) and the barbiturates, are desired by addicts and others for nonmedical use. The records of the Food and Drug Administration contain the stories of broken homes and human derelicts that the improper use of these drugs has caused. Other drugs in the prescription-only class may cause irreparable injury before the user knows that the drug is having any physiological effect upon him. But the present law, interpreted to reach these abuses existing in connection with the refilling of prescriptions, also prohibits the refilling of prescriptions for drugs that are not dangerous and are entirely suitable for use by a layman without medical supervision. Furthermore, if the refilling of prescriptions for dangerous drugs and drugs which require medical supervision in their use is to be controlled, the statute itself should contain express provisions providing for such controls.

The bill, as amended, meets this situation by providing that when drugs are prescribed which are safe and effective for lay use without medical supervision, and which could be bought freely over the counter without a prescription, the prescriptions may be freely refilled. But as to drugs which are habit-forming, or which are safe and efficacious only after medical diagnosis has been made or when medical supervision is exercised, and as to drugs which are restricted by new drug applications to use under medical supervision, the bill provides that

prescriptions cannot be refilled unless the prescriber has expressly authorized the refill. This authorization may be either written or oral, but if it is given orally the dispenser must promptly reduce the authorization to writing and file it.

SECTION BY SECTION EXPLANATION OF THE BILL, AS AMENDED

SECTION 1. AMENDMENT TO EXISTING LAW

The first section of the bill, as amended, proposes to rewrite section 503 (b) of the present law. At the present time, section 503 (b) merely provides for an exemption from certain labeling requirements in the case of drugs dispensed on written prescription. As proposed to be rewritten, section 503 (b) would contain paragraphs (1) to (6), inclusive, which are explained below:

Paragraph (1)—Prohibited acts

This paragraph provides that three types of drugs which are intended for human consumption shall be dispensed only under the following conditions:

(i) Upon a written prescription of a practitioner licensed by law to administer the drug, or

(ii) Upon an oral prescription of such practitioner which is reduced promptly to writing by the pharmacist and filed by him, or

(iii) By refilling any such written or oral prescription if such refilling is authorized by the prescriber either in the original prescription or by an oral order which is reduced promptly to writing by the pharmacist and filed by him.

The types of drugs to which these requirements are made applicable are specified in three subparagraphs, designated (A), (B), and (C).

Subparagraph (A) covers habit-forming drugs. Subparagraph (C) covers any new drug which, under other provisions of the act, is limited to use under professional supervision. No controversy has arisen as to these provisions.

Subparagraph (B) covers "dangerous" drugs, and describes them as any drug which—

> because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, has been determined by the Administrator * * * to be safe and efficacious for use only after professional diagnosis by, or under the supervision of, a practitioner licensed by law to administer such drug.

The standard here used is essentially the same as that used in regulations heretofore prescribed under the act. As used in such regulations the standard has been generally acceptable to the drug industry as shown in the testimony before the committee.

Subparagraph (B) provides that the Federal Security Administrator will have the duty of determining (on the basis of opinions generally held among qualified experts) the specific drugs covered by the standard, his determination being subject to judicial review as provided in paragraph (5).

Paragraph (1) provides that the act of dispensing a drug contrary to its provisions shall be deemed to be an act which results in the drug being misbranded while held for sale. The effect of this provision is to

make criminal, injunction, and seizure provisions of the act applicable to the dispensing of a drug in violation of the provisions of paragraph (1).

Paragraph (2)—Exemption from labeling requirements

This paragraph exempts drugs dispensed by filling or refilling a written or oral prescription of a licensed practitioner from most of the labeling and packaging requirements which ordinarily apply to drugs. To get the exemption, the container in which the prescription medicine is dispensed must bear a label containing the name and address of the dispenser, the serial number and date of the prescription or of its filling, the name of the prescriber, and, if stated in the prescription, the name of the patient, and the directions for use and cautionary statements, if any, contained in the prescription.

The exemption does not relax the prohibition against false or misleading labeling, the prohibition against selling an imitation drug, or offering a drug for sale under the name of another drug; nor does the exemption change the requirement that any drug containing insulin, penicillin, streptomycin, aureomycin, chloramphenicol, or bacitracin must be pretested and certified, or the requirement that any official drug must be packaged as required by the official compendium, or that any drug liable to deterioration must be packaged in accordance with regulations established under existing law. The exemption will not be applicable to any drug dispensed in the course of the conduct of the business of dispensing drugs pursuant to diagnosis by mail or otherwise without examination of the patient. The latter provision follows the existing law.

It is provided in paragraph (2) that the exemption provided thereby shall not apply to habit-forming, dangerous, and new drugs dispensed in violation of the prescription requirements of paragraph (1).

Paragraph (3)—Exemption from prescription requirements

This paragraph permits the Administrator by regulations to remove habit-forming and new drugs from the prescription requirement of paragraph (1) when that requirement is not necessary for the protection of the public health. These drugs are the ones covered by subparagraphs (A) and (C) of paragraph (1). This relaxation is necessary to permit the sale without prescription of drugs containing small amounts of habit-forming drugs as components, and to permit the sale of new drugs without prescription when that safeguard is unnecessary.

Paragraph (4)—Labeling of prescription drugs and over-the-counter drugs

This paragraph requires that any drug to which paragraph (1) applies must bear on its label the statement "Caution: Federal law prohibits dispensing without prescription." It also provides that a drug to which paragraph (1) does not apply shall be deemed to be misbranded if at any time prior to dispensing its label bears any statement which represents or implies that the dispensing of the drug without the prescription of a licensed practitioner is prohibited.

Paragraph (5)—Hearings and judicial review

This paragraph deals with the procedure to be followed in a case where an interested party desires to secure a formal hearing or judicial review with respect to a determination by the Administrator as to whether a drug is a "dangerous" drug according to the standard contained in subparagraph (B) of paragraph (1). This procedure is made available to contest either a proposed determination by the Administrator, to seek a determination that a drug which has already been listed should be removed from the list, or to seek to have placed on the list a drug which is not on the list.

For any of these purposes an interested person may file a petition with the Administrator. Where the petition is for the purpose of opposing a proposed determination that a drug is "dangerous", the filing of a petition will stay the operation of paragraph (1) with respect to the drug until a petition for judicial review can be filed, and interim relief sought, under section 10 (d) of the Administrative Procedure Act. This provision, together with the procedural safeguards of the Administrative Procedure Act, will insure that the Administrator cannot place a drug on the list until interested persons have had full opportunity to test the validity of the Administrator's action.

When a petition is filed stating reasonable grounds, the Administrator will be under a duty to give public notice of the proposal made in the petition and to give all interested persons a reasonable opportunity to present their views, orally or in writing, and it will be his duty to act on the petition as soon as is practicable. Any interested person who is dissatisfied with the Administrator's action may (if he files an objection to such action, stating reasonable grounds therefor, within 30 days after it is made public) demand and secure a public hearing before the Administrator for the taking of evidence of experts who are qualified by scientific training and experience to testify on the question of whether the drug in question is safe and efficacious for use only after professional diagnosis by, or under the supervision of, a practitioner licensed by law to administer the drug. As soon as practicable after the hearing, the Administrator must issue an appropriate order. The Administrator may make his order only after consideration of the whole record and in accordance with reliable, probative, and substantial evidence, and he will be required to make detailed findings of the facts on which he based his order.

The order of the Administrator will be subject to judicial review in accordance with the provisions of section 701 (f) and (g) of the Federal Food, Drug, and Cosmetic Act. These are the judicial review provisions which are now applicable to the review of orders issued under certain other provisions of the act. Such review will be by the appropriate circuit court of appeals of the United States, and may be had upon the filing of a petition with the court at any time prior to the ninetieth day after the issuance of the order by the Administrator. Review will be upon the basis of the "substantial evidence" rule which is the generally applicable provision for judicial review contained in the Administrative Procedure Act.

Paragraph (6)—Narcotics laws unaffected

This paragraph provides that nothing in subsection (b) shall be construed to relieve any person from any requirement prescribed by or under law with respect to narcotics or marihuana.

SECTION 2. EFFECTIVE DATE

This section of the bill provides that its provisions shall take effect 6 months after the date of its enactment into law. This postponement of the effective date of the legislation is deemed to be necessary in order that the Administrator will have time to take steps, before the legislation takes effect, with a view to determining which drugs are "dangerous" under the standard prescribed in subparagraph (B) of section 503 (b) (1).

CHANGES IN EXISTING LAW

In compliance with paragraph 2a of rule XIII of the Rules of the House of Representatives, changes in existing law made by the bill, as introduced, are shown as follows (existing law proposed to be omitted is enclosed in black brackets, new matter is printed in italics, existing law in which no change is proposed is shown in roman):

SECTION 503 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT

EXEMPTIONS IN CASE OF DRUGS AND DEVICES

SEC. 503. (a) The Administrator is hereby directed to promulgate regulations exempting from any labeling or packing requirement of this Act drugs and devices which are, in accordance with the practice of the trade, to be processed, labeled, or repacked in substantial quantities at establishments other than those where originally processed or packed, on condition that such drugs and devices are not adulterated or misbranded under the provisions of this Act upon removal from such processing, labeling, or repacking establishment.

[(b) A drug dispensed on a written prescription signed by a physician, dentist, or veterinarian (except a drug dispensed in the course of the conduct of a business of dispensing drugs pursuant to diagnosis by mail), shall if—

[(1) such physician, dentist, or veterinarian is licensed by law to administer such drug, and

[(2) such drug bears a label containing the name and place of business of the dispenser, the serial number and date of such prescription, and the name of such physician, dentist, or veterinarian,

be exempt from the requirements of section 502 (b) and (c), and (in case such prescription is marked by the writer thereof as not refillable or its refilling is prohibited by law) of section 502 (d).]

(b) A drug dispensed by filling or refilling a written or oral prescription of a practitioner licensed by law to administer such drug shall be exempt from the requirements of section 502, except paragraphs (a), (i) (2) and (3), (k), and (l), and the packaging requirements of paragraphs (g) and (h), if the drug bears a label containing the name and address of the dispenser, the serial number and date of the prescription, or of its filling, the name of the prescriber, and, if stated in the prescription, the name of the patient, and the directions for use and cautionary statements, if any, contained in such prescription. This exemption shall not apply to any drug dispensed in the course of the conduct of a business of dispensing drugs pursuant to diagnosis by mail or otherwise without examination of the patient. If the drug is intended for use by man and—

(1) is a habit-forming drug subject to the regulations prescribed under section 502 (d);

(2) has been found by the Administrator, after investigation and opportunity for public hearing, to be unsafe or ineffective for use without the professional diagnosis or supervision of a practitioner licensed by law;

(3) if an effective application under section 505 limits it to use under the professional supervision of a practitioner licensed by law, such exemption shall apply only if such drug is dispensed upon a written prescription of a practitioner licensed by law to administer such drug or upon an oral prescription of such practitioner which is reduced to writing and filed by the pharmacist, or is dispensed by refilling a prescription if such refilling is authorized by the prescriber in the original prescription or by oral order and such order is reduced to writing and filed by the pharmacist.

The Administrator may by regulation remove drugs subject to section 502 (d) and section 505 from the provision of this subsection when such requirements are not necessary for the protection of the public health.

A drug which is subject to clause (1), (2), or (3) of this subsection shall be deemed to be misbranded if at any time prior to dispensing its label fails to bear the statement "Caution: Federal law prohibits sale or dispensing without prescription".

The act of dispensing a drug contrary to the provisions of this subsection shall be deemed to be an act which results in the drug's being misbranded while held for sale.

Any interested person may file with the Administrator a petition proposing the addition to, or deletion from, the list of drugs promulgated by the Administrator in accordance with clause (2) hereof. Such petition shall set forth the proposal in general terms and shall state reasonable grounds therefor. The Administrator shall give public notice of the proposal and an opportunity for all interested persons to present their views thereon, orally or in writing, and as soon as practicable thereafter shall make public his action upon such proposal. At any time prior to the thirtieth day after such action is made public any interested person may file objections to such action, specifying with particularity the changes desired, stating reasonable grounds therefor and requesting a public hearing upon such objections. The Administrator shall thereupon, after due notice, hold such public hearing. As soon as practicable after completion of the hearing, the Administrator shall by order make public his action on such objections.

An order so issued by the Administrator may, within ninety days after its issuance, be appealed by any interested person in accordance with the provisions prescribed in section 701 (f) and (g) of this Act, except that an appeal from the Administrator's order issued hereunder shall be in the nature of a trial de novo, without presumptions in favor of either party to such appeal.

The provisions of this section of the Act shall not be applicable to drugs now included or which may hereafter be included within the classifications stated in section 3220 of the Internal Revenue Code (26 U. S. C. 3220), or to marijuana as defined in section 3235 (b) of the Internal Revenue Code (26 U. S. C. 328 (b)).

APPENDIX

FEDERAL SECURITY AGENCY,
Washington, April 30, 1951.

Hon. ROBERT CROSSER,
Chairman, Committee on Interstate and Foreign Commerce,
House of Representatives, Washington 25, D. C.

DEAR MR. CHAIRMAN: This letter is in response to your request of March 21, 1951, for a report on H. R. 3298, a bill to amend section 503 (b) of the Federal Food, Drug, and Cosmetic Act.

This bill is in substantially the same form as that introduced as H. R. 8904 in the Eighty-first Congress, second session, which this Agency endorsed. Section 503 (b) of the present law recognizes only written prescriptions, whereas the section as amended by the bill would recognize oral prescriptions as well, with the safeguard under certain circumstances that the pharmacist reduce the oral order to writing and file it. The present law does not provide a clear differentiation between those drugs which should be dispensed solely on prescription and those which may be sold over the counter. It is the intent of the bill to supply this deficiency by requiring the dispensing on prescription only of specified habit-forming drugs and those specifically designated in regulations or new drug applications which cannot be safely and effectively used without professional diagnosis and supervision. The bill provides that the labels of such drugs bear a caution against dispensing without prescription.

This Agency is sympathetic to the purposes of the bill. It would clarify the obligations of pharmacists, would promote the operations of all on the high standards now followed by the majority, and would afford better protection to the public health than the present law against abuses by a minority in dispensing highly potent drugs by over-the-counter sales or by refilling prescriptions without the knowledge and approval of the prescriber.

The bill contains, however, three new paragraphs beginning at line 15 of page 3 and continuing to line 14 of page 4. The most significant feature of the new paragraphs is a "trial de novo" (lines 12–14 on p. 4) in a United States court of appeals on appeals from the Administrator's orders. An outline of the procedure leading up to the proposed "trial de novo" is relevant. Clause (2) of new section 503 (b) requires that an opportunity for public hearing be afforded before the Administrator promulgates a list of drugs that are unsafe or ineffective for use without professional diagnosis and supervision and thus must therefore be dispensed only on prescription. This public hearing, it would seem, may be held under the informal rule-making procedure of section 4 of the Administrative Procedure Act. No appeal would lie at this stage from the resulting action of the Administrator (see Administrative Procedure Act, sec. 10).

The last paragraph on page 3 of the bill provides for a formal hearing and judicial review when any interested party disagrees with the order of the Administrator issued under clause 2. The procedural steps provided are as follows: (1) Any interested person may file a petition setting forth the proposal for addition to or deletion from the list of drugs, with a statement of reasonable grounds. (2) Public notice of the proposal and an opportunity to present views by interested parties are given. (3) A decision of the Administrator with respect to that proposal is made. (4) Objections to the decision may be filed within 30 days, with a request for a public hearing on such objections. (5) A hearing on the objections is held. The formal hearing provisions of sections 7 and 8 of the Administrative Procedure Act would apparently apply to that hearing. (6) An order is issued. This order is subject to judicial review in accordance with section 701 (f) and (g) of the Food and Drug Act, except that such review shall be "in the nature of a trial de novo, without presumptions in favor of either party to such appeal."

These provisions are in general patterned after section 507 (f) (21 U. S. C. 357 (f)) relating to the certification of antibiotic drugs. The Administrator's order with respect to objections filed by interested parties concerning his regulations under section 507 (f) is subject to the provisions of section 701 (f) and (g) (21 U. S. C. 371 (f) and (g)). Section 701 (f) provides that the findings of the Administrator as to the facts, if supported by substantial evidence, shall be conclusive. But the bill expands the scope of review. The bill directs that the "appeal" is to be in the nature of a "trial de novo" without presumptions in favor of either party to such appeal. The concept of a "trial de novo" at the appellate level departs radically from legislation governing the review of rules and regulations issued by administrative agencies, and goes beyond the require-

ments of the Administrative Procedure Act which was intended to bring uniformity to administrative proceedings and their judicial review. The scope of judicial review now embodied in section 10 (e) of the Administrative Procedure Act is that agency action shall be upheld where it is supported by "substantial evidence," but the court is directed to review the whole record in determining whether the evidence is substantial. This provision has recently been examined by the Supreme Court in *Universal Camera Corp.* v. *National Labor Relations Board*, decided February 26, 1951. The specific provision to this effect in section 701 (f) of the Federal Food, Drug, and Cosmetic Act, and its conformity to the Administrative Procedure Act, was judicially approved in *Willapoint Oysters* v. *Ewing* (174 F. 2d 676, cert. den. 338 U. S. 860).

The proposed bill, in contrast, would extend the function of the reviewing court beyond that contemplated by the Administrative Procedure Act. The appellate court in a "trial de novo" would become a trier of facts with respect to difficult questions of drug action, questions which are not at all suited for judicial determination but which require expert scientific knowledge for informed judgment. The determination of such a question is peculiarly within the expert competence of an administrative agency, yet the court would be expressly enjoined to attach no "presumptions" to its action, i. e., to give no weight to it. The Administrative Procedure Act has recognized the principle of deference to administrative expertise by providing for review as to the legal sufficiency of the evidence presented in support of a regulation, not a complete and needless retrial of the facts in an appellate court.[1]

There is serious question, moreover, as to the propriety of conferring the power to make a determination that is essentially legislative upon a "constitutional court." This was declared objectionable by the Supreme Court in *Federal Radio Commission* v. *General Electric Co.* (281 U. S. 464 (1930)) and in the cases there cited. In the General Electric case, the Radio Act of 1927 had authorized the court of appeals, after decision by the Commission, to take additional evidence, hear, review, and determine the appeal upon the record and the evidence, and alter or revise the decision appealed from—in short, a review de novo. While the opinion acknowledged that Congress may make the Court of Appeals for the District of Columbia a "superior and revising" agency, it concluded that the Supreme Court could not be invested with similar powers. In this connection, it should be noted that section 701 (f) (1) of the Food and Drug Act, which is incorporated in the bill by reference, would confer jurisdiction on the Supreme Court to review decisions of the courts of appeals. Moreover, under the bill proceedings for judicial review could be filed in the court of appeals for the circuit in which the petitioner resides or has his principal place of business, which, in most cases, would be outside the District of Columbia. Such other courts of appeals, being "constitutional courts," would be subject to the same disability in this respect as the Supreme Court.

The legislative history of the present act reveals that Congress was confronted with a similar problem as to the scope of review of administrative regulations and rejected the solution now proposed. As reported out with an amendment by the House Committee on Interstate and Foreign Commerce after passage by the Senate, S. 5, Seventy-fifth Congress, contained a special review provision in section 701 (f) permitting anyone appealing from a regulation to adduce additional evidence before a district court, and further providing that the court might take such further action as "justice may require" (H. Rept. No. 2139, 75th Cong., 3d sess., pp. 11–12). The Supreme Court, in *Federal Security Administrator* v. *Quaker Oats Co.* (318 U. S. 218 (1943)) explained the elimination of this provision:

"* * * before enactment, the conference committee substituted for these provisions those which became section 701 (f) of the act. While under that section the Administrator's regulations must be supported by findings based upon 'substantial evidence' adduced at the hearing, the Administrator's findings as to the facts if based on substantial evidence are conclusive. In explaining these changes the chairman of the House conferees stated on the floor of the House that 'there is no purpose that the court shall exercise the functions that belong to the executive or the legislative branches' (83 Congressional Record, p. 9096)."

The conference committee further noted, with respect to the review provided in section 701 (f) (S. Rept. No. 2716, 75th Cong., 3d sess.):

"The type of judicial review provided in the agreement is as broad as the Constitution permits in the case of review by a constitutional court. It is to be noted that the function of the Secretary in making regulations and orders to

[1] In any event, the use of the word "trial" in the bill is in itself a misnomer. In all probability the drafters intended to have a review on the record and not a trial de novo.

carry them out is legislative in character * * *. Judicial review of the Secretary's action to determine if there was substantial evidence to support the finding, and of course, upon constitutional questions, may be had."

To permit a review by trial de novo at the level of the court of appeals would not only impede and hamper the enforcement program with respect to the most dangerous drugs, but would burden these courts with a legislative function which, it appears likely, they may not constitutionally be called upon to perform.

This bill also authorizes oral prescriptions which are reduced to writing and filed by the pharmacist. It does not require that the physician confirm or agree to confirm the prescription in writing. In this, it departs from the bill which we previously endorsed. We believe that at the very least the physician should agree to confirm his oral prescriptions in writing within 72 hours, and that he should not be entirely freed from his responsibility to confirm because the pharmacist reduced the telephone order to writing.

We therefore recommend that the bill, with the above-suggested amendment, with the deletion of the excepting provision in lines 12–14 on page 4, and with certain clarifications and technical amendments which we should like to suggest at the appropriate time, be enacted by the Congress.

The Bureau of the Budget advises that there is no objection to the submission of this report to your committee.

Sincerely yours,

OSCAR R. EWING, *Administrator.*

APRIL 30, 1951.

Hon. ROBERT CROSSER,
Chairman, Committee on Interstate and Foreign Commerce,
House of Representatives, Washington, D. C.

MY DEAR MR. CHAIRMAN: This is in response to your request for the views of the Department of Justice concerning the bill (H. R. 3298) to amend section 503 (b) of the Federal Food, Drug, and Cosmetic Act.

Section 502 of the Federal Food, Drug, and Cosmetic Act (21 U. S. C. 352) sets forth the various circumstances under which drugs and devices will be deemed to be misbranded. Section 503 (b) (21 U. S. C. 353 (b)) specifies certain exemptions with respect to drugs dispensed on written prescriptions.

The bill would amend section 503 (b) so as to provide that a drug dispensed by filling or refilling a written or oral prescription shall be exempt from the requirements of section 502, except with respect to certain packaging requirements and those provisions of the section which provide that a drug shall be deemed to be misbranded if its labeling is false or misleading in any particular or if it is an imitation of another drug or if it is offered for sale under the name of another drug, and except with respect to the provisions of the act dealing with insulin and the various antibiotics covered by the statute. The measure provides, however, that such exemption shall prevail only if the drug bears a label containing the name and address of the dispenser, the serial number and date of the prescription or of its filling, the name of the prescriber and, if stated in the prescription, the name of the patient, and the directions for use and cautionary statements, if any, contained in the prescription.

Separate provision is made if the drug is intended for use by man, and is (1) a habit-forming drug subject to the regulations prescribed under section 502 (d) (21 U. S. C. 352 (d)), or (2) has been found by the Federal Security Administrator to be unsafe or ineffective for use without the professional diagnosis or supervision of a practitioner licensed by law, or (3) if an effective new drug application under section 505 (21 U. S. C. 355) limits it to use under the professional supervision of a licensed practitioner. In such event the exemption is to apply only if the drug is dispensed upon a written prescription or upon an oral prescription which is reduced to writing and filed by the pharmacist, or is dispensed by refilling a prescription if such refilling is authorized by the prescriber in the original prescription or the oral order and such order is reduced to writing and filed by the pharmacist. A drug which falls within the three categories mentioned immediately above will be misbranded if at any time prior to its being dispensed its label fails to bear the statement "Caution: Federal law prohibits sale or dispensing without prescription."

The bill also provides that the act of dispensing the drug contrary to the provisions of the bill shall be deemed to be an act which results in the drug's being misbranded while held for sale. This would insert into the Federal Food, Drug, and Cosmetic Act the theory, based on regulations, pursuant to which the Food and Drug Administration has recommended prosecution of druggists who sell

without prescriptions, drugs bearing the so-called prescription legend and which have not been removed from the immediate containers in which they were shipped in interstate commerce. Such a sale by a druggist would be in violation of section 301 (k) (21 U. S. C. 331 (k)).

The bill also provides a procedure whereby any interested person may file a petition with the Federal Security Administrator proposing the addition to or deletion from the list of drugs found to be unsafe or ineffective for use in accordance with clause (2) of section 503 (b). Upon the filing of such a petition, the Administrator is required to give public notice of the proposal and a hearing thereon, and as soon as practicable thereafter shall make public his action upon such proposal. Any interested person may file objections to such action and request a public hearing upon such objections. The Administrator shall thereupon after due notice hold such public hearing and as soon as practicable thereafter by order make public his action on such objections. The order of the Administrator may within 90 days after its issuance be appealed to the court of appeals in accordance with the provisions prescribed in section 701 (f) and (g) of the Act (21 U. S. C. 371 (f) and (g)), except that such appeal shall be in the nature of a trial de novo without presumptions in favor of either party to such appeal.

The bill also provides that its provisions shall not apply to drugs now included or which may hereafter be included within the classification stated in section 3220 of the Internal Revenue Code or to marijuana as defined in section 3238 (b) thereof.

Whether the bill should be enacted involves a question of policy concerning which this Department prefers not to make any recommendation. There are certain features of the measure, however, concerning which the committee may wish to give further consideration.

The bill provides for two public hearings in connection with a proposal for the addition to or deletion from the list of drugs found to be unsafe in accordance with the provisions of clause 2. A public hearing is provided for on the original proposal, and again provided for in connection with objections to the action of the Administrator upon the proposal. It would seem that the one public hearing on the original proposal would be sufficient.

The bill also provides for an appeal from the order of the Administrator. It is assumed that the order referred to is that made after the public hearing on the objections to the previous action of the Administrator. The review proceeding is to be in accordance with the provisions of section 701 (f) and (g) of the act, except that the appeal shall be in the nature of a trial de novo. It will be noted, however, that the review proceedings in section 701 are confined to questions of law. The court is given jurisdiction to affirm the order complained of or to set it aside in whole or in part. If the order refuses to issue, amend, or repeal a regulation and such order is not in accordance with law, the court shall by its judgment order the Administrator to take action with respect to the matter, in accordance with law. In a de novo proceeding the court ordinarily has the power and function to make its own findings and judgment. Such a trial contemplates not only the record before the Administrator but the testimony of additional witnesses if desired. No such procedure is contemplated under section 701. The provision for a trial de novo would be incompatible with the review procedure provided for and leaves an ambiguity and doubt as to what the function of the appellate court would be. In addition, such a proceeding would appear to make the appellate court a revising agency and its action in the nature of an administrative decision. A question arises as to whether such a function is within the judicial power conferred upon Federal courts by the Constitution. Compare *Radio Commission* v. *General Electric Co.* (281 U. S. 464).

It might be desirable to consider the question of review in connection with the action of the Administrator in designating unsafe drugs under clause (2). It is believed that a review from such a determination in accordance with the procedure in section 701, would fully protect the rights of any person adversely affected since the Supreme Court has recently held that in considering the question of whether an order of this nature is supported by substantial evidence, the appellate court shall review the whole record.

The Director of the Bureau of the Budget has advised that there is no objection to the submission of this report.

Yours sincerely,

PEYTON FORD,
Deputy Attorney General.

ADMINISTRATIVE OFFICE OF THE UNITED STATES COURTS,
Washington 13, D. C., March 29, 1951.

Hon. ROBERT CROSSER,
House Office Building, Washington, D. C.

DEAR CONGRESSMAN CROSSER: I have compared the bill about which you have written me on March 22, 1951, to amend section 503 (b) of the Federal Food, Drug, and Cosmetic Act (H. R. 3298) with the present provision of the statute. The statute deals with the exemption from the requirements of the Federal Food, Drug, and Cosmetic Act in relation to the labeling of drugs handled in interstate commerce of drugs that are dispensed on a written prescription of a licensed physician, dentist, or veterinarian. The bill would make more detailed and specific the safeguards against abuse of the exemption from the provisions of the general statute.

The only feature of the bill that my office may qualify me to discuss is the provision in the next to the last paragraph of subsection (b) of section 503 of the statute as proposed to be amended (p. 4, lines 8 to 14) and especially the last clause on lines 11 to 14 of the printed bill. This section provides for appeals from orders of the Federal Security Administrator adding to or deleting from the list of drugs promulgated by him as "unsafe or ineffective for use without the professional diagnosis or supervision of a practitioner licensed by law" (clause 2, p. 2, lines 12 to 16 of the printed bill). It defines the procedure on appeal in general by reference to section 701 (f) (g) of the statute (21 U. S. C. 371 (f) (g)). These subsections provide that appeals from the orders of the Administrator may be filed in the United States court of appeals for the circuit in which the person taking the appeal resides or has his principal place of business. The pending bill would not change the court which would have jurisdiction to review orders of the Administrator in reference to the subject matter affected. That court would continue to be the court of appeals for the circuit.

The exception at the end of the paragraph would, however, make an important change from the present statute in respect of the procedure on review. Sections 701 (f) (g) of the present statute (21 U. S. C. 371 (f) (g)) prescribe that when a review is taken the review shall be had upon a transcript of the record and proceedings before the Administrator. "The findings of the Administrator as to the facts, if supported by substantial evidence, shall be conclusive." The paragraph referred to of the pending bill would change the practice and make the appeal "in the nature of a trial de novo, without presumptions in favor of either party to such appeal."

The Judicial Conference of the United States under which I act has not considered the particular bill and, therefore, I am not in a position to express an official opinion in regard to it, although the conference is on record in opposition to the procedure of a trial de novo by a three-judge court for review of the orders of administrative agencies. I would point out that the provision that appeals from the order of the Administrator shall be in the nature of a trial de novo, reverses what has been for 20 years or more a uniform trend in the Federal Government to provide for the hearing and decision of appeals from orders of administrative agencies by the courts of appeals upon the record made before the agencies. This procedure has been repeatedly provided for by the Congress, most recently by a law passed at the end of the Eighty-first Congress and approved December 29, 1950, in relation to the review of certain orders of the Federal Communications Commission, the Secretary of Agriculture, and the United States Maritime Commission (Public Law 901 of the 81st Cong.). That law originated in a recommendation of such legislation by the Judicial Conference.

The considerations underlying the act are stated in House Report No. 2122 of the Eighty-first Congress. The report states that review by the court of appeals of orders of administrative agencies upon the record made before the agencies "has important advantages in simplicity and expedition" over a trial de novo by a three-judge court. From the report I quote pertinent portions as follows:

"First, the submission of the cases upon the records made before the administrative agencies will avoid the making of two records, one before the agency and one before the court, and thus going over the same ground twice * * *."

"Second, in many cases in which hearing in the district courts by panels of three judges is now required there will be a large saving of judicial time and energy. It is generally recognized that three-judge courts are not well adapted for conducting hearings. The necessity of holding conferences whenever questions arise in the course of the proceedings, as they repeatedly do in relation to such matters as the admissibility of evidence, very much slows the trial. In addition the proceeding takes the time of three judges, whereas one would be sufficient at this

preliminary stage of the case. The method of review prescribed by the proposed bill would secure the collaboration of three judges at the stage where it is useful, namely, in the decision without consuming their time unnecessarily in the preceding phases of the case."

While the practice which was changed by Public Law 901 of the Eighty-first Congress in reference to the agencies there concerned was trial de novo by a three-judge district court and the trial de novo on appeal from orders of the Administrator in the field of the pending bill would be such a trial by three judges of a court of appeals, all the disadvantages of trial de novo by a three-judge court referred to in the report of the last Congress would apply. There would be the same going over the ground twice in two records, the same difficulty inevitable in a court of three judges in conferring upon questions of the admission of evidence and other interlocutory matters arising during the proceedings, thus slowing the trial, and the same absorption of the time of three judges where one would be sufficient. It may be added that in no case at present, with perhaps an occasional extraordinary exception, does a court of appeals sit as a trial court or hear evidence. The present statute which the pending bill would change, provides that even in those instances in which the court allows the petitioner to adduce additional evidence, such evidence shall be taken before the Administrator and adduced to the court rather than taken by the court of appeals directly.

The precedent which would be set by the pending bill of having the hearing on review conducted by the court of appeals as a trial de novo would be a radical departure. It would be contrary to the general judgment in reference to the effective procedure for the review of orders of administrative agencies as expressed in the report and law of the last Congress which have been cited. Such a change of method at this time when there is serious congestion in a number of Federal courts would tend to increase the present difficulties and delays in the handling of the judicial business.

Sincerely yours,

HENRY P. CHANDLER.

ADMINISTRATIVE OFFICE OF THE UNITED STATES COURTS,
Washington 13, D. C., April 12, 1951.

Hon. ROBERT CROSSER,
House Office Building, Washington, D. C.

DEAR CONGRESSMAN CROSSER: In further reference to the bill to amend section 503 (b) of the Federal Food, Drug, and Cosmetic Act (H. R. 3298) about which you inquired of me on March 22, 1951, I would point out that the provision for judicial review of actions of the Administrator contained in the next to the last paragraph of subsection (b) of section 503 of the statute as proposed to be amended (p. 4, lines 11 to 14 of the bill) is in conflict with the criterion prescribed in such long-considered and deliberate enactments of the Congress as the Administrative Procedure Act approved June 11, 1946 (60 Stat. 237), and the Labor Management Relations Act, 1947, commonly known as the Taft-Hartley Act approved June 23, 1947 (61 Stat. 136). The legislative policy in reference to the weight to be given to the decisions of administrative agencies by the courts and the evidence necessary to sustain them were recently considered at length by the Supreme Court of the United States and reviewed in detail in the case of *Universal Camera Corporation* v. *National Labor Relations Board* (No. 40 at the present term of the court). At the same time the court rendered a brief corollary opinion applying the same standard of review in the case of *National Labor Relations Board* v. *Pittsburgh Steamship Co.* (No. 42 at the present term of court). Briefly, the development of the standard to be applied by the courts on the review of orders of administrative agencies as set forth in the opinion in the case of the Universal Camera Corp., supra, is this:

The original National Labor Relations Act, commonly known as the Wagner Act, provided in section 10 (e) in reference to the judicial review of decisions of the National Labor Relations Board that "The findings of the Board as to the facts, if supported by evidence, shall be conclusive" (49 Stat. 449, 454, 29 U. S. C. 160 (e)).

The Supreme Court in *Washington, V. & M. Coach Co.* v. *Labor Board* (301 U. S. 142) construed "evidence" to mean substantial evidence. In the early years of application of the Wagner Act the opinion became current that on judicial review of an order of the National Labor Relations Board, if there was in the record made before the Board evidence which taken by itself would justify the Board's decision, that would be enough to satisfy the test of substantial evidence irrespec-

tive of other parts of the record. The Supreme Court in its opinion supra stated that there were expressions in some of the opinions of that Court which were cited (*Labor Board* v. *Waterman Steamship Corp.*, 309 U. S. 206; *Labor Board* v. *Bradford Dyeing Assn.*, 310 U. S. 318; and *Labor Board* v. *Nevada Consolidated Copper Corp.*, 316 U. S. 105) that whether or not so contemplated gave color to that view.

The doctrine stated brought criticism which was reflected in the passage in 1940 of the Walter-Logan bill. Even so, the bill adopted the test for judicial review of orders of administrative agencies which was expressed in the Wagner Act as construed by the Supreme Court, that the findings of fact by an agency could be set aside by a court if "not supported by substantial evidence." President Roosevelt vetoed the bill partly because it limited too strictly the administrative process and partly because an experienced committee appointed by the Attorney General of the United States was then engaged in a study of the actual operation of the administrative process. That committee submitted its final report in 1941. The majority report observed that there was dissatisfaction with the fact-finding procedures then being used by administrative bodies but concluded that it would be inadvisable to depart from the test on judicial review of substantial evidence which then applied to the review of orders of administrative agencies. Three members of the committee, however, registered dissent on the ground that the recommendations of the committee did not go far enough to correct defects in the procedures of administrative agencies. Among other things, the dissenting members of the committee recommended as one principle of judicial review applicable generally to administrative agencies, that review should extend to "findings, inferences, or conclusions of fact unsupported, upon the whole record, by substantial evidence." The Supreme Court in the Camera Corp. case supra states that reference to the whole record appears for the first time in the recommendation of the minority of the Attorney General's committee. The opinion of the Court goes on to state that this idea found its way into the Administrative Procedure Act enacted in 1946 (pp. 6 to 8 of the opinion in the Camera Corp. case supra). So the Administrative Procedure Act in section 10 (e) provided that on judicial review the court should hold unlawful and set aside agency action if—

"(5) unsupported by substantial evidence in any case subject to the requirements of sections 7 and 8 or otherwise reviewed on the record of an agency hearing provided by statute; or (6) unwarranted by the facts to the extent that the facts are subject to trial de novo by the reviewing court. In making the foregoing determinations the court shall review the whole record or such portions thereof as may be cited by any party, and due account shall be taken of the rule of prejudicial error" (60 Stat. 244, 5 U. S. C. 1009 (e)).

It is important to note that the statute requires that a court in determining whether or not an order of an administrative agency under review is "unsupported by substantial evidence" shall "review the whole record or such portions thereof as may be cited by any party." In short, in adopting the Administrative Procedure Act the Congress did not do away with the presumption on review in favor of the decision of an administrative agency if supported by substantial evidence, but made it unmistakably clear that the reviewing court in determining whether there was substantial evidence to justify the conclusion must take into account the whole record, or any portions cited by any parties, which doubtless would be all the pertinent parts.

The Supreme Court in its recent opinion in the Camera Corp. case points out that the amendment of the Wagner Act by the Taft-Hartley Act adopted in effect the same standard for judicial review of decisions of the National Labor Relations Board, that was prescribed for administrative agencies generally by the Administrative Procedure Act. The provision of the Taft-Hartley law appears in section 10 (e) that the findings of the National Labor Relations Board "with respect to questions of fact if supported by substantial evidence on the record considered as a whole shall be conclusive" (29 U. S. C., 1946 ed., Supp. III, 160 (e)).

The Supreme Court points out in the Camera Corp. case that the effect of the Administrative Procedure Act and the Labor-Management Relations Act, 1947, has been to require reviewing courts to carry the scrutiny of decisions of administrative agencies further than was thought in some legal circles to be necessary prior to the passage of the Administrative Procedure Act. Upon this the Court said:

"Whether or not it was ever permissible for courts to determine the substantiality of evidence supporting a Labor Board decision merely on the basis of evidence which in and of itself justified it, without taking into account contra-

dictory evidence or evidence from which conflicting inferences could be drawn, the new legislation definitively precludes such a theory of review and bars its practice. The substantiality of evidence must take into account whatever in the record fairly detracts from its weight. This is the clear meaning of the reference in both statutes to 'the whole record.' Committee reports and the adoption in the Administrative Procedure Act of the minority views of the Attorney General's Committee demonstrate that to enjoin such a duty on the reviewing court was one of the important purposes of the movement which eventuated in that enactment."

The Supreme Court is careful to point out in its recent decision that it does not mean that in reviewing the decision of an administrative agency a court shall consider the record before the agency de novo and substitute its judgment for that of the agency. The court expressed its meaning upon the necessity of considering "the whole record" as follows:

"To be sure, the requirement for canvassing 'the whole record' in order to ascertain substantiality does not furnish a calculus of value by which a reviewing court can assess the evidence. Nor was it intended to negative the function of the Labor Board as one of those agencies presumably equipped or informed by experience to deal with a specialized field of knowledge, whose findings within that field carry the authority of an expertness which courts do not possess and therefore must respect. Nor does it mean that even as to matters not requiring expertise a court may displace the Board's choice between two fairly conflicting views, even though the court would justifiably have made a different choice had the matter been before it de novo. Congress has merely made it clear that a reviewing court is not barred from setting aside a Board decision when it cannot conscientiously find that the evidence supporting that decision is substantial, when viewed in the light that the record in its entirety furnishes, including the body of evidence opposed to the Board's view."

The provision of the pending bill that the review before a court of appeals of a decision of the Administrator under the Federal Food, Drug, and Cosmetic Act "shall be in the nature of a trial de novo, without presumptions in favor of either party" is plainly contrary to the policy of the Congress deliberately adopted in the Administrative Procedure Act after years of discussion and consideration and followed in the Taft-Hartley law. That policy is that the judical review of orders of administrative agencies shall be upon the record made before the agencies and not in the nature of a second trial, and that if the action of the agency is supported by substantial evidence when considered in the light of the entire record, it shall stand. It would seem that the Congress might hesitate to change a policy based upon experience and finally crystallized in outstanding legislative acts, as the pending bill would do.

Sincerely yours,

HENRY P. CHANDLER.

MINORITY REPORT

have any objections to the provisions of the bill which for the filling and refilling of oral or telephone prescrip- resent law does not recognize oral prescriptions, and we e majority that, for the benefit of the public, the phy- retail druggist, the filling and refilling of oral prescrip- oper safeguard should be permitted. We also approve refilling of prescriptions dispensing dangerous drugs, uthorized orally or in writing by the physician. We e enactment of the foregoing provisions of the bill is as should go at this time in making changes in the present ect to the labeling and dispensing of drugs. The re- sions would make basic changes in the method of de- ch drugs are dangerous and may be sold only on pre- which drugs are safe and may be sold over the counter. present method, which leaves this determination to the be left unchanged except that a proper standard to be ermining whether a drug is dangerous should be incor- statute.

BASIS FOR OBJECTIONS

bjectionable feature of the bill lies in the provision ive the Federal Security Administrator the power to category in which a drug should be placed. In other ministrator would decide by the issuance of regulations ch could be sold only upon prescription and, by the sion, those which could be sold over the counter without This we believe to be a dangerous delegation of au- Federal Security Administrator and one that is wholly Moreover, instead of solving the problems of the public. gist and the physician, it will add to present difficulties ureaucratic regulation.

there is some degree of confusion today arising from s by drug manufacturers. In some instances one com- l a drug for prescription sale only, while another will drug for over-the-counter use. But there is a remedy on under existing law. If a drug manufacturer places drug on the market without a proper caution label scription use, he may be prosecuted criminally, and the ay seize his product. Similarly, if a drug manufacturer ess drug for prescription use only he may likewise be inst for erroneous labeling. If a druggist dispenses a manufacturer has not properly labeled he is not subject while acting in good faith.

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and (4) articles intended for use as a
articles.

But such is far from being the case. ggist could not safely dispense any egulations of the Federal Security g contrary to the regulations of the rt to prosecution and the defense of to him.

ISTS' DILEMMA

his bill became a law on its effective s would be subject to regulation. ggist in the country would have to lministrator's regulations from the is entire inventory and relabel his egulations. This initial task would average druggist, but his troubles h, he would have to review the r from day to day and week to week complying with the Administrator's

blems that beset the small-business ther bureaucratic regulation. For al regimentation upon the already ness man is not only unreasonable

the present system of determining ess on a case-by-case basis is much remedy, which would create more We have been constrained to dis- le this report because we are con- nstitutes an excessive and entirely ry power to the Federal Security

HE DRUG INDUSTRY

efills and of oral prescriptions from Federal Food, Drug, and Cosmetic rancement of a plan to regulate the rted empowers the Administrator articles included within the broad ich he has determined to be "safe rofessional diagnosis by, or under icensed by law to administer such

in the Federal Food, Drug, and recognized in the United States Pharmacopoeia of the United y; (2) articles intended for use in tment, or prevention of disease in other than food) intended to affect he body of man or other animals; component of any of the foregoing

This definition includes substances, compounds, mixtures, and fabrications of all kinds and forms used, or intended to be used, for the purposes above stated. There was testimony at the hearings that there are approximately 30,000 such "drugs." Any such drug intended for use by man which "on the basis of opinions generally held among experts qualified by scientific training and experience to evaluated the safety and efficacy of such drug" the Administrator determines "to be safe and efficacious for use only after professional diagnosis by, or under the supervision of, a practitioner licensed by law to administer such drug," shall be thereby restricted to sale only on prescription.

The bill grants the Administrator authority to separate all drugs into two classes—prescription and over the counter. Notwithstanding the majority report's references to "dangerous" and "potent" drugs, this power is not confined to them. There is little, if any, uncertainty about them. This power will find its greatest exercise in the wide field of conflicting opinion. There, as the testimony shows, "there are literally thousands of different drug items." This large field was described by the Administrator, in his testimony before the committee, as the "twilight zone." The power to govern it administratively would in time, amount to an over-all control of the manufacture, distribution, and administration of drugs. And, in the exercise of it, the Administrator would have greatly to do not only with the manufacture and distribution of drugs, but with the practice of pharmacy and medicine.

EFFICACY OF DRUGS

This control is widened by the use of the words "efficacy" and "efficacious". The majority report labors a distinction between the Administrator having the power "to determine which drugs are 'efficacious' or 'effective'" and his having the power to determine whether they "can be used efficaciously without professional diagnosis or supervision." The undersigned do not find the distinction to be as clear and as easily discernible as the majority professes. Stated either way, the power granted to the Administrator is vast in scope, and, in administrative application and interpretation, would in time become larger and embrace both statements of the authority.

The majority illustrates with the drug quinidine sulfate. More illustrative, however, is a statement in the Administrator's testimony. Asked whether there is any possibility under the bill that a prescription would be required for a refill of aspirin, the Administrator stated:

> Well, as of today, I would say "No," but I think you have to recognize that under this bill you might have an Administrator who would call a hearing to put aspirin on the list of dangerous drugs. If he held that aspirin was a dangerous drug and that was appealed to the circuit court of appeals and they upheld it, then you would be in that situation.

For further illustration, attention may be drawn to the word "diagnosis." Drugs which the Administrator determines are not safe or efficacious until "after professional diagnosis" are to be restricted to prescription sale. It is well known that there are some "experts" who entertain the view that hardly any drug is either "safe" or "efficacious" without professional diagnosis; that the layman is not competent to diagnose his ailments; and that, without being able to diagnose, he is all the more unable to prescribe for himself.

SOCIALIZED MEDICINE

In the opinion of the undersigned, there is no doubt that the bill as reported jeopardizes the traditional right of self-medication and choice of remedies. Self-medication is not confined to so-called "patent medicines." It embraces use by the public of medicaments or "drugs" which are sold over the counter and which may be purchased without prescription, whether or not they are advertised direct to the public by newspaper, magazine, and radio. The Federal Food, Drug, and Cosmetic Act, as enacted in 1938, recognized the right of self-medication, and one of the committee reports stated that it was not the purpose of the act to restrict self-medication, but to make it safe.

Thousands of articles of a medicinal or remedial nature are now lawfully available to the people and may be purchased without the expense of prescriptions—fees to doctors and prescription prices at the drug store. The undersigned believe that the bill as reported will increasingly over the years restrict the number and nature of drugs available to the public on over-the-counter sale, and thus will gradually and substantially increase the cost of medication. This bill, therefore, could very well become a handmaiden of socialized medicine in that as the costs of medical care are increased there will be a corresponding demand by the people for governmental relief.

CONTROL BY LICENSE

No grant of administrative power as wide in scope and as far-reaching in effect and implication as that in this bill has heretofore been proposed for the regulation of the drug industry. The grant of power in this bill is such as to transform, as to drugs, the Federal Food, Drug, and Cosmetic Act from a control by statutorily defined requirements to a control by license.

This proposed control is subject only to limited, uncertain, and impracticable restraint. It is no restraint to say, as the bill does, that the Administrator is to make his determination "on the basis of opinions generally held among experts qualified by scientific training and experience to evaluate the safety and efficacy" of drugs. Rather, it is lax to permit administrative authority to be constituted and rights of citizens determined on "opinions generally held" by persons unnamed in and unknown to the statute, to be selected and qualified at later times by the Administrator himself.

Practically, this bill shifts the burden of proof from the Administrator, who would assert the authority, to the citizen, who challenges it. The bill provides that the Administrator makes his determination merely on the basis of opinions of experts. If the producer or distributor of one of the drugs whose sale is restricted challenges the Administrator's determination, the bill provides that he "may file with the Administrator a petition proposing * * * a modification of a determination made or proposed to be made by the Administrator * * *." Then a sequence of time-consuming and expensive steps are begun:

(1) The Administrator gives public notice of the proposal contained in the petition and gives to "interested" persons an opportunity to present views orally or in writing;

(2) Thereafter, the Administrator makes public his action on the proposal;

(3) Within 30 days after he makes such action public, any "interested" person may file with the Administrator objections to such action, stating changes proposed, grounds therefor, and requesting a public hearing "for the taking of evidence of experts who are qualified by scientific training and experience to testify as to the question of whether the drug in question is safe and efficacious for use only after professional diagnosis by, or under the supervision of, a practitioner licensed by law to administer such drug";

(4) The Administrator shall then give notice and hold a public hearing;

(5) Thereafter, the Administrator shall make his determination and issue an order;

(6) The order shall then be subject to "judicial review in accordance with the provisions of section 701 (f) and (g)" of the Federal Food, Drug, and Cosmetic Act, which are (in part):

(f) A summons and petition served upon the Administrator, whereupon the Administrator must certify and file in the court the transcript of the proceedings and the record on which the Administrator based his order;

(g) A certified copy of the transcript of the record and proceedings shall be furnished by the Administrator to any interested party at his request, and payment of the cost thereof.

(7) Review of the record by a United States Court of Appeals. "The findings of the Administrator as to the facts, if supported by substantial evidence, shall be conclusive."

CONCLUSION

We desire to affirm our support of that part of the proposed legislation referred to in the first paragraph of this report. Our objections to the remaining provisions of the bill are grounded on the tremendous grant of unnecessary power in the hands of the Federal Security Administrator.

LEONARD W. HALL,
JOSEPH P. O'HARA.
JOHN B. BENNETT.

INDIVIDUAL MINORITY VIEW

The undersigned, while concurring in the minority report in opposition to the vast delegation of authority to the Administrator, strongly feels that if this bill is to become law there should be a provision for an appeal and a trial de novo in the United States district court.

Not having had the time to submit my individual views to the other signers of the minority report, I therefore take the responsibility of submitting these additional views.

An appellant who desires a review of the record by a United States court of appeals, is confronted with the law, with reference to the decisions of the Federal Security Administrator, as follows:

> The findings of the Administrator as to the facts, if supported by substantial evidence, shall be conclusive.

The majority of the committee takes the position that the Administrator's action under the bill in listing a drug as "dangerous," thereby limiting it to prescription sale, is subject to judicial review which will assure those affected against abuse of the power granted the Administrator.

With this conclusion I vigorously disagree.

The bill provides for judicial review under the familiar "substantial evidence" rule, which permits the courts to overturn administrative action only if the abuse of administrative authority is of a most flagrant character.

In recent years there has been increasing dissatisfaction with the "substantial evidence" rule, under which the findings of fact made by the administrative agency are conclusive if supported by substantial evidence.

The following typical statements by the Supreme Court give an idea as to the limitations under which the courts have operated in reviewing administrative action under the "substantial evidence" rule:

> * * * (The) court * * * will not consider the expediency or wisdom of the order, or whether, on like testimony, it would have made a similar ruling. *Int. Com. Comm.* v. *Union Pacific R. R.*, 222 U. S. 541.
>
> The order of the Commission * * * was not arbitrary but sustained by substantial, though conflicting, evidence. The courts cannot settle the conflict nor put their judgment against that of the rate-making body * * *. *Int. Com. Comm.* v. *Louis. & Nash. R. R.* 227, U. S. 88, 100.

If the record contained any substantial evidence to support the administrative fact findings, the courts often have felt obligated to sustain the administrative action without reference to how heavily such evidence may have been outweighed by the countervailing evidence in the record. Under this limitation the courts cannot set aside administrative action even when it is clearly contrary to the manifest weight of the evidence.

The type of judicial review leaves much too large an area in which the administrative agency has a free hand to exercise, in an unfair

and unjust manner, the power of life and death over important elements of the economic structure of the country.

The majority report strongly suggests that recent Supreme Court decisions (*Universal Camera Corp.* v. *N. L. R. B.* and *Labor Board* v. *Pittsburgh S. S. Co.*) have made a change in the law which insures operation of the "substantial evidence" rule in such manner that full protection will be given by the courts against unjustified administrative action. These cases held that the courts, in determining whether the administrative action is supported by substantial evidence, are under a duty to make that determination after consideration of the whole record before the administrative agency. No one can say at this time whether, or to what extent, these cases will actually change anything so far as scope and character of judicial review is concerned. There is good ground for believing that they merely state what the law always has been. There is nothing in these cases to indicate that the Supreme Court would regard it as proper for a reviewing court to weigh the evidence in the record and, on the basis of its appraisal of the evidence, reach its own independent judgment as to what the administrative action should have been and take appropriate action to insure that the administrative action conforms to the judgment of the court.

Mr. Justice Frankfurter, speaking for the Court in the Universal Camera case, made the following statement which indicates the narrow limits of judicial review under the law as it is interpreted in that case:

> To be sure, the requirement for canvassing "the whole record" in order to ascertain substantiality does not furnish a calculus of value by which a reviewing court can assess evidence. * * * Nor does it mean that even as to matters not requiring expertise a court may displace the Board's choice between two fairly conflicting views, even though the court would justifiably have made a different choice had the matter been before it de novo.

In the opinion of the undersigned, these cases have no important bearing on the fundamental issue here involved.

The bill as introduced would have authorized judicial review of the Administrator's action in a proceeding in the nature of a trial de novo. In the opinion of the undersigned, that type of judicial review would afford a proper judicial check on administrative abuses. Largely on the basis of testimony presented to the committee by Judge Stephens of the United States Court of Appeals for the District of Columbia, the committee has rejected this proposal of the introduced bill.

To the extent that the testimony criticized provision for a de novo trial in a United States court of appeals, the objections made by Judge Stephens are probably sound, but no convincing argument has been made against providing for de novo review in an appropriate United States district court. It may be true that review by district courts, if provided for in the case of administrative action of every type, would make some increase, to a limited extent, of cases in United States district courts. However, the proposal in the introduced bill did not extend to all cases of administrative action, but only to review of the action of the Federal Security Administrator, under this proposed legislation, in listing a drug as a "dangerous" drug. This would not require any increase in the number of United States district judges, in my opinion. Furthermore, even if it did, that would be a

small price to pay for judicial review which would effectively control abuses in the exercise of the vast administrative power which this bill proposes to grant to the Federal Security Administrator.

The majority report, apparently on the basis of views stated in letters from the Federal Security Administrator and the Deputy Attorney General of the United States, expresses doubts as to the constitutionality of any provision providing for judicial review of the Administrator's action in a de novo proceeding, on the ground that this would seek to have Federal "constitutional" courts exercise an improper function—that is, one which is legislative or administrative in character, and therefore "nonjudicial."

The views expressed in the letters referred to are based upon a decision rendered by the Supreme Court in the General Electric case (281 U. S. 464) which was decided in 1930. That case held that the Supreme Court (being a "constitutional" court, i. e., one which, because created under the judiciary article of the Constitution, can exercise only "judicial" powers) could not be vested with the power to act as a "superior and revising" administrative agency in reviewing a decision of the Court of Appeals of the District of Columbia (which is not a "constitutional" court) in a case, arising under the Radio Act of 1927, in which the latter court had exercised de novo review of action taken by the Federal Radio Commission. This, the court said, was because it could exercise "judicial powers only," and could not "exercise or participate in the exercise of functions which are essentially legislative or administrative."

The argument is that since United States courts of appeals and United States district courts are "constitutional" courts the principle of the General Electric case applies to them, although this specific question has never been judicially decided. However, even if this is so, de novo review of the Administrator's action would not be barred by the principle of the General Electric case. This is because of the difference in the nature of the function which the court would exercise.

In the General Electric case the basic question in issue was whether the public convenience and necessity would be served by granting an application for renewal of a broadcasting license. Under this bill, the question in issue would be whether a particular drug is—

> because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use * * * (determined) * * * on the basis of opinions generally held among experts qualified * * * to evaluate the safety and efficacy of such drug * * * to be safe and efficacious for use only after professional diagnosis by, or under the supervision of, a practitioner licensed by law to administer such drug.

It will be seen at a glance that the bill calls for the application of a standard, or test, which is not of the same character as that involved in the General Electric case. The latter case called for the exercise of broad judgment and discretion in deciding whether renewal of a broadcasting license would serve "the public convenience and necessity." It is not surprising that the Supreme Court took the view that substitution of its judgment for that of the agency on that question would have involved exercise of a nonjudicial function.

However, under the bill, no similar judgment or discretion would have to be exercised by the court. In applying the standard, or test, provided for by the bill a court would be determining whether a particular drug was or was not included within its terms. The function

of the court would not be essentially different from that exercised by courts every day. It would merely call for application of a statutory standard to the facts of a particular case.

In this connection, it is important to bear in mind that the standard written into the bill is essentialy the same as that now contained in the regulation (prescribed under section 502 (f) of the act) which differentiates "dangerous" drugs (which may be sold only on prescription) from those drugs which (if they bear adequate directions for use) may be safely sold over the counter. In criminal prosecutions, and in seizure and injunction proceedings, involving alleged misbranding, the outsome of the case may depend upon the application by the court to the facts of the case of this standard prescribed in the regulation. If the courts exercise a "judicial" function in applying this standard in criminal, seizure, and injunction actions, how can it be reasonably contended that a court would be called upon to exercise a "nonjudicial" function in applying essentially the same standard in de novo review of the Administrator's action?

Furthermore, it was urged before the committee that this same standard be written into the bill as the basis for case-by-case judicial decision as to which drugs are "dangerous" and which drugs are not. No one suggested that that proposal would have required the courts to exercise a "nonjudicial" function.

The need for trial de novo is emphasized by the narrowness of review of administrative proceedings by the appellate courts. In an increasing number of cases the courts are declaring their impotence to review the findings of fact.

Particularly is this true where the administrative decision is of a quasi-judicial nature, as in the instances of appeals from the Federal Trade Commission, which is a fact-finding body. The courts have repeatedly held that they are bound by the Federal Trade Commission's judgment as to the quality and sufficiency of evidence. Such evidence may consist of biased testimony—*Segal* v. *Federal Trade Commission* (142 Fed. (2d) 255); incompetent evidence—*Bene* v. *Federal Trade Commission* (299 Fed. 468); and the testimony of selected experts—*E. Griffith Hughes, Inc.* v. *Federal Trade Commission* (77 Fed. (2d) 886). In the Segal case the court observed that a part of the testimony was "obviously biased" and said:

> Even so, if the Commission wished to rely upon such testimony, we may not intervene, whatever might be our own indisposition to accept what he said.

The courts refuse on appeal to weigh the evidence. They hold that they are bound by the Commission's findings, if supported by evidence, despite the fact that the weight may be to the contrary. Thus, they need read only the Commission's side of the case and if there is evidence to support the findings, the record to the contrary may be ignored.

The principles of a trial de novo are outlined in my opinion, by Chief Justice D. Lawrence Groner of the Circuit Court of Appeals for the District of Columbia in a letter to the Attorney General—report of the Committee on Administrative Procedure, Seventy-ninth Congress, page 248:

> The correct decision of this question is one of immense importance. It should, in my opinion, be considered by Congress in the light of the real and true purposes which the founders of our Government sought to achieve for themselves and their

posterity. These were free action, free enterprise, free competition. They believed that equal justice between man and man and between citizen and state was one of the impartial rewards which encouraged to efforts that produced great and lasting results. Therefore, they made no provision for exemptions from legal duty. What they did provide for was that there should be no oppression, no exaction by tyranny, no spoliation of private right by public authority, and that there should be a fair, honest, effective government to maintain the things which were thought to be the prerogatives of every individual man.

As in the case of the Federal Trade Commission, the Federal Security Administrator is not only a regulator but he will adjudicate issues of fact between the Government and the citizen as a judicial tribunal. The Administrator, under this bill, will be asked to determine the question of fact of some 30,000 drug items—

> because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use * * * (determined) * * * on the basis of opinions generally held among experts qualified * * * to evaluate the safety and efficacy of such drug * * * to be safe and efficacious for use only after professional diagnosis by, or under the supervision of, a practitioner licensed by law to administer such drug.

In the light of the above-quoted section of this bill, the Administrator will be called upon to make decisions of fact "on the basis of opinions generally held among experts qualified." It may be upon the decision of one expert who is opposed by many experts, upon testimony which may be biased or unbiased; and yet, under existing decisions, even if the Administrator made his decision on testimony which was obviously biased, that decision of the Administrator, for all practical purposes, would be final without a trial de novo.

In the light of the Supreme Court decisions and the sweeping scope of the powers granted the governmental administrative agency, unless there is to be complete administrative absolutism, it is obvious that both the Government and the individual should have a "day in court."

JOSEPH P. O'HARA.

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Calendar No. 898

82D CONGRESS
1st Session

SENATE

REPORT
No. 946

AMENDING SECTIONS 303 (C) AND 503 (B) OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT

OCTOBER 12 (legislative day, OCTOBER 1), 1951.—Ordered to be printed

Mr. HUMPHREY, from the Committee on Labor and Public Welfare, submitted the following

REPORT

[To accompany H. R. 3298]

The Committee on Labor and Public Welfare, to whom was referred the bill (H. R. 3298) to amend section 503 (b) of the Federal Food, Drug, and Cosmetic Act, as amended, having considered the same, report favorably thereon with amendments and recommend that the bill, as amended, do pass.

The amendments are as follows:

(1) On page 3, line 5, strike out the words "or otherwise without examination of the patient" and insert in lieu thereof a comma.

(2) On page 3, lines 19–22, strike out the words "or any other statement which represents or implies that the dispensing of the drug without the prescription of a licensed practitioner is prohibited."

(3) On page 4, between lines 5 and 6, insert a new section 2, to read as follows:

SEC. 2. Subsection (c) of section 303 of the Federal Food, Drug, and Cosmetic Act, as amended, is amended by inserting before the period a semicolon and the following: "or (4) for having violated section 301 (b), (c), or (k) by failure to comply with section 502 (f) in respect to an article received in interstate commerce to which neither section 503 (a) nor section 503 (b) (1) is applicable, if the delivery or proffered delivery was made in good faith and the labeling at the time thereof contained the same directions for use and warning statements as were contained in the labeling at the time of such receipt of such article."

(4) On page 4, line 6, strike out the figure "2" and insert in lieu thereof the figure "3."

INTRODUCTION

This bill amends the Federal Food, Drug, and Cosmetic Act to deal more directly and realistically with the labeling and dispensing of drugs that may be sold only upon the prescription of licensed practitioners. It has a twofold objective: (1) to protect the public from abuses in the sale of potent prescription drugs; and (2) to relieve retail

EXHIBIT B

pharmacists and the public from burdensome and unnecessary restrictions on the dispensing of drugs that are safe for use without the supervision of a physician. The committee believes that the bill, as amended, will serve to eliminate much confusion and dissatisfaction caused by ambiguities in the present provisions of the act, and will benefit drug manufacturers, retail druggists, medical practitioners, and the public.

In its consideration of this bill, the Committee has had the benefit of careful study of its provisions by its standing Subcommittee on Health. The subcommittee carefully and thoroughly explored the need for such legislation at this time, and examined the manner in which the provisions of the bill are adapted to deal with the serious problems which have been shown to exist in connection with the labeling and dispensing of both "prescription" and "over-the-counter" drugs. Hearings on the bill were held before the subcommittee from September 11 through September 13, 1951. Favorable action on the bill was urged at the hearing by the Federal Security Administrator and by the Food and Drug Administration, the agency of the Government that administers and enforces the Federal Food, Drug, and Cosmetic Act. In addition, virtually all segments of the drug industry, including the principal associations of drug manufacturers, the retail druggists, and the licensed pharmacists were represented at the hearing and submitted testimony which clearly shows that this bill is necessary legislation and will do much to make the Act a fairer and more effective instrument for protecting the public against abuses in the labeling and dispensing of drugs. A representative of the American Medical Association testified at the hearing in support of the bill.

The hearing held before the subcommittee developed the fact that while there was virtually unanimity of opinion of those who testified as to the need for basic changes in the law governing the labeling and dispensing of "prescription" drugs, there were two principal issues in controversy.

1. The first area of controversy was over a proposal to authorize the Federal Security Administrator to list by name or class the "dangerous" drugs that may be sold only on prescription. The subcommittee had before it for consideration at the time of the hearing, not only this bill, which has been passed by the House of Representatives, but also the companion Senate bill (S. 1186), and amendments in the nature of a substitute therefor, introduced by Senator Humphrey. The principal difference between the bill as passed by the House of Representatives and Senator Humphrey's amendments in the nature of a substitute, had to do with the requirement under which, as part of the definition of so-called dangerous drugs, an administrative determination would have been necessary thus to classify a drug. The amendments in the nature of a substitute for S. 1186 also set forth detailed procedures, including administrative hearings to be followed in connection with the making of administrative determinations referred to, together with provisions for judicial review of such determinations.

Prior to the hearing, the provisions for administrative listing of so-called dangerous drugs were vigorously supported by the National Association of Retail Druggists, and equally vigorously opposed by the several associations of drug manufacturers, including the American Pharmaceutical Manufacturers' Association, the American Drug Man-

ufacturers Association, and the Proprietary Association. At the hearing, however, a statement was submitted on behalf of all four of these associations, indicating an agreement on their part that the controversial provisions for administrative listing of so-called dangerous drugs might be eliminated. The four associations, at the same time, proposed two new amendments to the bill. This agreement had the effect of eliminating one of the principal areas of controversy, particularly in view of the fact that the subcommittee was assured by the Food and Drug Administration and the Federal Security Administrator that the bill, while not in their view the best solution, would be workable in the form proposed under the agreement. The subcommittee recommended to the Committee on Labor and Public Welfare, therefore, that the provisions of the House bill which omit the administrative listing provisions, rather than the provisions of the amendments in the nature of a substitute for S. 1186 which include such provisions, be favorably reported to the Senate. The subcommittee further recommended, in reporting favorably on the House bill, that the bill be amended to include the two amendments proposed by the associations of retail druggists and drug manufacturers under the agreement referred to above. The intent and effect of these amendments are discussed hereafter in this report.

2. The other principal area of controversy which developed at the hearing arose with respect to certain language of the bill which was objected to by the representative of a firm engaged in selling through the mail to epileptic patients living throughout the United States a medication comprised principally of phenobarbital. Although the language in question was included in the legislation as originally introduced in both the House of Representatives and the Senate, in the bill as reported to the House of Representatives by the House Interstate and Foreign Commerce Committee and in the bill as passed in the House of Representatives, no issue had been raised concerning this language prior to the hearing before the subcommittee. The subcommittee, however, felt that the language might safely be omitted from the bill. Accordingly, it proposed, and the committee recommends, that this language be stricken. The effect of this amendment is discussed elsewhere in this report.

WHAT THE BILL DOES

As has been pointed out, the bill amends the Federal Food, Drug, and Cosmetic Act so that its provisions will be better adapted to deal realistically with the labeling and dispensing of drugs that may be sold only upon the prescription of licensed practitioners. Its provisions are remedial in the sense that they are intended to protect the public from abuses in the sale of potent prescription medicines. They will also relieve retail pharmacists of unnecessary restrictions on the dispensing of drugs that are safe for use without medical supervision.

Prescription drugs

The bill provides a statutory definition of prescription drugs; it expressly forbids their sale without a prescription; it specifies how they are to be labeled both at the time of interstate shipment and at the time of ultimate dispensing; and it prohibits unauthorized refilling of prescriptions for them.

There are three classes of drugs covered by the statutory definition. The first includes the habit-forming drugs subject to section 502 (d) of the present statute. These are such drugs as the barbiturates. The third class includes all new drugs restricted to prescription sale by effective new-drug applications under section 505 of the present statute. There is no controversy whatever about these two classes. The second class includes any drug which "because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, is not safe for use except under the supervision of a practitioner licensed by law to administer such drugs."

This definition of so-called dangerous drugs is contained in paragraph (b) (1) (B) of the bill. It is substantially the same as the administrative definition now contained in the regulations issued by the Federal Security Administrator under the provisions of the Federal Food, Drug, and Cosmetic Act. The proposed definition, however, omits the reference to "efficacious" for use, as well as "safe" for use, without the supervision of a medical practitioner in order to be eligible for over-the-counter sale. This omission is not intended to mean that the only matter to be considered in applying the definition is whether or not a particular drug is poisonous.

The word "safe," as used in the definition, is intended to have its ordinary meaning. For example, nontoxic drugs like quinidine sulfate, intended for heart disease, or penicillin, for infections, are not safe for self-medication because their unsupervised use may indirectly cause injury or death. The language of the definition clearly shows that toxicity is only one factor to be considered by the courts in determining whether a particular drug is safe for use without medical supervision. The definition requires the court to consider also other potentialities for harmful effect, the method by which the drug is used, and the collateral measures that may be necessary in order to use the drug safely. When this language is given judicial interpretation consistent with the over-all purpose of the Federal Food, Drug, and Cosmetic Act to protect the public health it will effectively restrict to prescription sale all drugs that require professional supervision for their use.

In order to give this general definition a more precise meaning so that it may be applied with greater uniformity by the drug trade the Administrator can exercise the authority he has under section 701 (a) of the Federal Food, Drug, and Cosmetic Act to issue interpretative regulations. It is to be understood that the inclusion of the statutory definition does not, of course, in any way derogate from the Administrator's authority to interpret and enforce the definition through the issuance of any regulations necessary or appropriate to protect the public from indiscriminate dispensing of drugs over the counter when they may be unsafe for use without the supervision of a practitioner licensed by law to administer such drugs.

As previously stated, the committee considered S. 1186 together with H. R. 3298. S. 1186 would have authorized the Federal Security Administrator to list by name or class the drugs which he considered within the statutory definition. The grant of such administrative authority was objected to as an unnecessary regulation of the drug industry, and the committee concluded that administrative listing is not necessary at this time. It was felt that the statutory definition,

together with the authority to make interpretative regulations, could bring an end to the existing confusion in drug labeling and that uniformity can be achieved through cooperative efforts of the drug industry and the Food and Drug Administration working under the statutory plan. If the present confusion is not ended by this legislation it will then be time enough to consider the need for the administrative listing approach.

All drugs covered by the three classifications of prescription drugs must bear a label containing the statement "Federal law prohibits dispensing without prescription." This gives the retail druggist clear notice that he will be in violation of the Federal Food, Drug, and Cosmetic Act if he dispenses any drug so labeled without a prescription. This bill also specifies what information must be contained upon the label of the package dispensed to the patient. That label must contain the name and address of the dispenser, the serial number and date of the prescription or of its filling, the name of the prescriber, and, if stated in the prescription, the name of the patient, and the directions for use and cautionary statements, if any, contained in the prescription.

This bill strengthens the controls over the habit-forming barbiturates. The problems of misuse of these drugs to the detriment of the public—especially of young people—are growing and must be controlled in the public interest. The bill requires that they be sold only on prescription and forbids unauthorized refills of prescriptions for them. In this, it is a definite and clear step forward. It is felt, however, that these drugs pose a special problem not common to all drugs because they are desired by addicts for nonmedical use. This will call for their special treatment, and the committee wishes it understood that in recommending the passage of this bill, as amended, it does so with the knowledge that further legislative consideration must be given to adequate barbiturate controls.

The bill does not relieve any person from any requirements of law, now existing or hereafter adopted, with respect to drugs covered by the narcotic control laws. Paragraph (5) of section 1 makes this clear.

Oral prescriptions

The present law does not recognize the practice of dispensing drugs on oral prescriptions. The committee feels that in this respect the law needs modification and clarification for the convenience of the public, the retail druggist, and the physician. The filling and refilling of prescriptions upon oral or telephone orders with proper safeguards should be permitted, and this bill gives statutory recognition to the practice of telephone dispensing. It permits oral prescriptions for all drugs. However, in the case of habit-forming drugs, dangerous drugs, and new drugs limited to prescription sale, an oral prescription would have to be reduced promptly to writing and kept on file by the pharmacist. The oral order may be communicated to the dispenser by the prescriber himself or under his express authority.

Oral prescriptions for habit-forming drugs

The committee believes that the term "oral prescription," as used in the bill in connection with habit-forming drugs to which section 502 (d) of the act applies, should be given a construction which will assure that these drugs are used only upon the express order of a practitioner licensed by law to administer them. In fact, certain of

these drugs, such as narcotics subject to the Harrison Narcotics Act may be dispensed only on a written prescription of a licensed practitioner, and this requirement is expressly preserved by the bill. (See par. (5) of the new sec. 503 (b).) The public interest clearly requires that other habit-forming drugs be dispensed and used only under the close and immediate supervision of a licensed practitioner. Accordingly, it is the intention of the committee that the term "oral prescription" as applied to these drugs, means an order communicated orally to the pharmacist by a practitioner licensed by law to administer such drugs, expressly prescribing such a drug, which is reduced promptly to writing and filed by the pharmacist. The Food and Drug Administration, within the limitations of its staffing, can check pharmacists' records to make sure that all habit-forming drugs sold are accounted for by prescriptions on file. The pharmacist, before he dispenses any such drug on oral order, must obtain satisfactory evidence, on the basis of consultation with the licensed practitioner or otherwise, that the order has been expressly authorized in each case by such practitioner.

The Federal Security Agency may adopt regulations needed for the efficient enforcement of this provision, and may find it desirable to require special records for any habit-forming drugs dispensed so that pharmacists and enforcement officials alike can readily detect any possible abuses of the oral prescription privilege extended for such drugs.

Refilling prescriptions

The bill, as amended, deals expressly with the troublesome problem of refilling prescriptions. Under the present law a drug dispensed by refilling a prescription without the knowledge or consent of the prescriber is misbranded and the dispenser is liable to criminal prosecution. The committee concluded that these provisions are too stringent and should be modified. There is no reason why the law should prohibit the refilling of prescriptions for drugs that are not dangerous and are suitable for use by a layman without medical supervision. The bill provides that prescriptions for such drugs may be freely refilled. But, here again, as to drugs which are habit-forming, or which are dangerous, or which are restricted by new drug applications to use under medical supervision, the bill requires that prescriptions may be refilled only with the prescriber's express authorization. This authorization may be either written or oral, but if it is given orally the dispenser must promptly reduce it to writing and keep it on file.

The provisions relating to the refilling of prescriptions are needed to meet a serious public health problem which has arisen from the indiscriminate refilling of prescriptions for dangerous and habit-forming drugs. A witness for the Food and Drug Administration cited cases in which death had occurred as a consequence of unauthorized prescription refills. The use of dangerous and habit-forming drugs must be under the supervision of the prescribing physician. This bill is intended to require that the licensed practitioner, if he has not authorized the refill in writing, be consulted by the pharmacist and the refill be authorized by such practitioner before any prescription for a drug that is limited to prescription sale may be refilled.

EFFECT OF COMMITTEE AMENDMENTS

Amendment (1) was proposed by a firm engaged in selling through the mails to epileptic patients living throughout the United States a medication comprised principally of phenobarbital. Other provisions of the bill, to which the firm did not object, clarify and simplify the provisions of existing law regarding the labeling, sale, and dispensing of habit-forming and other dangerous drugs that should be sold only on prescription. These provisions are adequate to enable the Food and Drug Administration to compel such firms through appropriate court action, if necessary, to operate in a manner consistent with the public interest. The committee is aware of the obvious dangers to the public interest in the sale of barbiturates, including phenobarbital, without immediate and close medical supervision. The Food and Drug Administration has a responsibility in connection with the elimination of such dangers. This bill greatly strengthens the Administration's hand in discharging that responsibility.

The other two amendments were proposed by the combined drug trade in a statement signed by the National Association of Retail Druggists, the American Pharmaceutical Manufacturers' Association, the American Drug Manufacturers Association, and the Proprietary Association.

Amendment (2) was recommended because the associations felt the language it strikes out was of uncertain meaning and added nothing of importance to the bill. In any event, should a person place a statement on the label of a drug entirely safe for self-medication representing or implying that dispensing it without a prescription is prohibited by Federal law, that drug would be misbranded under the provision of law, section 502 (a), which forbids false or misleading labeling statements. Striking the language objected to does not relieve any manufacturer, regardless of the way in which he does business, from compliance with the requirement of section 502 (f) that all drugs not limited to prescription sale must bear adequate warnings and adequate directions for use telling the purchasing public what the drug is to be used for and how it is to be taken to accomplish the beneficial effects it is intended to have.

Amendment (3) was proposed to emphasize the fact that the responsibility for preparing adequate directions for use and appropriate warnings against misuse in the labeling of drugs that may be sold without a prescription is upon the manufacturer and not the retail druggist. It does nothing more than free the retail druggist of responsibility for supplementing the labeling of some manufacturers' drugs to give the public adequate directions for use and warnings against misuse. The druggist could rely in good faith upon the manufacturers' labeling for compliance with these requirements of the existing law. The amendment offers the druggist no protection against violations which arise if he sells a dangerous drug covered by paragraph (1) of the bill without meeting the prescription requirements.

Amendment (4) is a technical renumbering amendment.

EFFECTIVE DATE

Section 3 of the amended bill provides that its provisions shall take effect 6 months after the date of its enactment. This postponement

of the effective date is considered necessary to permit manufacturers to meet the new labeling requirements.

SECTIONAL ANALYSIS

Section 1 of the bill amends the Federal Food, Drug, and Cosmetic Act by substituting for subsection (b) of section 503, relating to the labeling and dispensing of prescription drugs, a new subsection defining drugs that may be dispensed only on prescription and specifying the conditions under which such drugs may be dispensed.

Prescription drugs

Under paragraph (1) of the new subsection (b) prescription drugs are defined as drugs intended for use by man which fall within any one of three different categories. In limiting prescription drugs to those intended for use by man this new subsection differs from the present law, which refers to prescription drugs to include not only those dispensed on prescription of physicians and dentists, but also those dispensed on prescription of a veterinarian. Under the committee bill, drugs intended for use under the supervision of a veterinarian will not require a prescription, although it will be possible under section 502 (f) to exempt such drugs from adequate directions for use if they are to be used by or under the supervision of a veterinarian. In the absence of any exempting regulations, these drugs will be subject to the labeling and dispensing requirements of the act applicable to over-the-counter drugs.

The three categories of prescription drugs defined as such in the bill are: (*a*) habit-forming drugs to which section 502 (d) of the act relating to drugs containing any narcotic or hypnotic substance, including barbituric acid, or habit-forming chemical derivatives thereof, is applicable; (*b*) drugs which, because of their toxicity or other potentiality for harmful effect, or the methods of their use, or the collateral measures necessary to their use, are not safe for use except under the supervision of a practitioner licensed by law to administer such drugs; or (*c*) drugs which are limited by an effective application under section 505 of the act, relating to new drugs, to use under professional supervision.

Included in the first of these three categories are not only the habit-forming narcotics and chemical derivatives thereof, but also barbituric acid and its habit-forming derivatives, such as amytal, phenobarbital, pentobarbital, and the like. This category includes all of the drugs and derivatives thereof specified in section 502 (d) of the act and the regulations thereunder. Dispensing of these drugs must not only comply with the provisions of the bill, but also must conform to the requirements of that section, and the interstate label must bear the name and quantity or proportion of the habit-forming drug or derivatives and in juxtaposition therewhit the statement: "Warning—May be habit forming."

The second category of prescription drugs, defined in subparagraph (B) of paragraph (1) of the new subsection (b) includes the so-called dangerous drugs. As noted elsewhere in this report, the phrase "not safe," as used in this subparagraph, is intended to have its ordinary meaning. Furthermore, in determining whether a drug is safe for use without medical supervision, there must be taken into consideration

not only the drug's toxicity, but also other potentialities for harmful effect, the method by which it is used, and the collateral measures necessary to its safe use. The broad language of the definition contained in this subparagraph is intended to comprehend all drugs that in fact should be administered under medical supervision in order to insure their safe use. Such difficult borderline cases as may arise under this definition can be dealt with under the interpretative and rule-making power provided for in section 701 (a) of the act.

The third category of drugs defined as "prescription" drugs includes all new drugs restricted to prescription sale by effective new drug applications under section 505 of the act.

Written and oral prescriptions and refills

Paragraph (1) of the new subsection (b) also provides that a "prescription" drug (any drug falling in any one of the three categories referred to above) shall be dispensed only (1) upon a written prescription of a practitioner licensed by law to administer such drug, or (2) upon an oral prescription of such a practitioner, communicated by him or under his express authority to the pharmacist, if such prescription is promptly reduced to writing and filed by the pharmacist, or (3) by refilling any such written or oral prescription if such refilling is authorized by or under the express authority of the practitioner either in the original prescription or by oral order, which is reduced promptly to writing and filed by the pharmacist. The provisions with respect to oral prescriptions and refills do not apply, however, in the case of narcotics subject to the Internal Revenue Code (Harrison Narcotic Act), since subparagraph (5) of the new subsection (b) expressly safeguards the provisions of that act, and under those provisions and the regulations of the Bureau of Narcotics such drugs may be dispensed only on written prescription. Also, as pointed out elsewhere, with respect to other habit-forming drugs, oral prescriptions and refills are limited to situations in which the pharmacist obtains satisfactory evidence, on the basis of consultation with a licensed practitioner or otherwise, that the prescription or refill has been expressly authorized by such practitioner. A violation of the prescription requirements of paragraph (1) of the new subsection (b) is, under the provisions of this paragraph, deemed to be an act which results in the drug being misbranded while held for sale.

Labeling of prescription drugs

Paragraph (2) of the new subsection (b) provides that a drug dispensed on prescription shall be exempt from the provisions of the act relating to the misbranding of drugs except those which specify that a drug shall be deemed to be misbranded if its labeling is false or misleading in any particular (sec. 502 (a)), if it is an imitation of another drug or is offered for sale under the name of another drug (sec. 502 (i) (2) and (3)), if it is, or purports to be, or is represented as a drug composed wholly or partly of insulin or of penicillin or certain other antibiotics except under certain conditions (sec. 502 (k) and (l)). These provisions continue to apply to any drug subject to the act, whether sold over-the-counter or on prescription. Similarly, the packaging requirements set forth in section 502 (g) and (h) apply to all such drugs. Prescription drugs must, however, bear at the time of dispensing a label containing the name and address of the dispenser,

the serial number and the date of the prescription or of its filling, the name of the practitioner, if stated in the prescription the name of the patient, and the directions for use and cautionary statements, if any, stated in the prescription. The exemption provided for by this paragraph does not apply to any drug dispensed in the course of the conduct of a business of dispensing drugs pursuant to diagnosis by mail, or to a drug dispensed in violation of paragraph (1) of the subsection.

Exempt narcotics and similar drugs

Under paragraph (3) of the new subsection (b) the Administrator may by regulation remove habit-forming drugs, as defined in section 502 (d), and new drugs, from the prescription requirements contained in paragraph (1) of the subsection when these requirements are not necessary for the protection of the public health.

Prescription legend

Paragraph (4) of the new subsection requires that, in addition to the labeling requirements in the case of prescription drugs specified in paragraph (2) of the subsection, the interstate label on such drugs must bear the statement "Caution: Federal law prohibits dispensing without prescription." On the other hand, over-the-counter drugs are forbidden to bear a label containing this caution statement. A prescription drug, the label on which does not bear the specified caution statement, is deemed to be misbranded. So, too, is an over-the-counter drug, the label on which bears this or a substantially similar statement.

Narcotics and marihuana

Paragraph (5) of the new subsection provides that compliance with the requirements of the bill does not relieve any person from any other requirement prescribed by or under authority of law with respect to drugs now or hereafter within the classifications defined in the Harrison Narcotic Act (sec. 3220 of the Internal Revenue Code, 26 U. S. C. 3220), or marihuana, as defined in section 3238 (b) of the Internal Revenue Code (26 U. S. C. 3238 (b)).

Good faith defense for retail druggists

Section 2 of the bill amends section 303 of the act, which specifies the penalties applicable to violations of the act. It adds to the several defenses available under subsection (c) of section 303 a new defense which has the effect of relieving from liability because of misbranding under section 502 (f) of the act any dispenser who makes delivery or proffers delivery of a drug in good faith if the labeling on such drug at the time of such delivery or proffered delivery contained the same directions for use and warning statements as were contained in the labeling at the time of receipt of the drug by such dispenser. This defense, however, is not applicable in the case of a drug which, in accordance with the practice of the trade, is to be processed, labeled, or repacked in substantial quantities at establishments other than those where originally processed or packed, and is not applicable to a prescription drug.

Effective date

Section 3 contains an effective date provision. In order to enable the drug industry to adapt its operations to the requirements specified in the bill, and to give the Food and Drug Administration time in

which to develop procedures necessary to implement administration of the bill, it is provided that the provisions of the bill will not go into effect until 6 months have elapsed after the date of its enactment.

CHANGES IN EXISTING LAW

In compliance with subsection 4 of rule XXIX of the Standing Rules of the Senate, changes in the existing law made by the bill are shown as follows: (Existing law proposed to be omitted is enclosed in black brackets; new matter is printed in italics, existing law in which no change is proposed is shown in roman).

FEDERAL FOOD, DRUG AND COSMETIC ACT

PENALTIES

SEC. 303. (a) Any person who violates any of the provisions of section 301 shall be guilty of a misdemeanor and shall on conviction thereof be subject to imprisonment for not more than one year, or a fine of not more than $1,000, or both such imprisonment and fine; but if the violation is committed after a conviction of such person under this section has become final such person shall be subject to imprisonment for not more than three years, or a fine of not more than $10,000, or both such imprisonment and fine.

(b) Notwithstanding the provisions of subsection (a) of this section, in case of a violation of any of the provisions of section 301, with intent to defraud or mislead, the penalty shall be imprisonment for not more than three years, or a fine of not more than $10,000, or both such imprisonment and fine.

(c) No person shall be subject to the penalties of subsection (a) of this section, (1) for having received in interstate commerce any article and delivered it or proffered delivery of it, if such delivery or proffer was made in good faith, unless he refuses to furnish on request of an officer or employee duly designated by the Administrator the name and address of the person from whom he purchased or received such article and copies of all documents, if any there be, pertaining to the delivery of the article to him; or (2) for having violated section 301 (a) or (d), if he establishes a guaranty or undertaking signed by, and containing the name and address of, the person residing in the United States from whom he received in good faith the article, to the effect, in case of an alleged violation of section 301 (a), that such article is not adulterated or misbranded, within the meaning of this Act, designating this Act, or to the effect, in case of an alleged violation of section 301 (d), that such article is not an article which may not, under the provisions of section 404 or 505, be introduced into interstate commerce; or (3) for having violated section 301 (a), where the violation exists because the article is adulterated by reason of containing a coal-tar color not from a batch certified in accordance with regulations promulgated by the Administrator under this Act, if such person establishes a guaranty or undertaking signed by, and containing the name and address of, the manufacturer of the coal-tar color, to the effect that such color was from a batch certified in accordance with the applicable regulations promulgated by the Administrator under this Act; *or (4) for having violated section 301 (b), (c) or (k) by failure to comply with section 502 (f) in respect to an article received in interstate commerce to which neither section 503 (a) nor section 503 (b) (1) is applicable, if the delivery or proffered delivery was made in good faith and the labeling at the time thereof contained the same directions for use and warning statements as were contained in the labeling at the time of such receipt of such article.*

EXEMPTIONS IN CASE OF DRUGS AND DEVICES

SEC. 503. (a) The Administrator is hereby directed to promulgate regulations exempting from any labeling or packing requirement of this Act drugs and devices which are, in accordance with the practice of the trade, to be processed, labeled, or repacked in substantial quantities at establishments other than those where originally processed or packed, on condition that such drugs and devices are not adulterated or misbranded under the provisions of this Act upon removal from such processing, labeling, or repacking establishment.

[(b) A drug dispensed on a written prescription signed by a physician, dentist, or veterinarian (except a drug dispensed in the course of the conduct of a business of dispensing drugs pursuant to diagnosis by mail), shall if—

(1) such physician, dentist, or veterinarian is licensed by law to administer such drug, and

(2) such drug bears a label containing the name and place of business of the dispenser, the serial number and date of such prescription, and the name of such physician, dentist, or veterinarian,

be exempt from the requirements of section 502 (b) and (c), and (in case such prescription is marked by the writer thereof as not refillable or its refilling is prohibited by law) of section 502 (d).]

(b) (1) A drug intended for use by man which—

(A) is a habit-forming drug to which section 502 (d) applies; or

(B) because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, is not safe for use except under the supervision of a practitioner licensed by law to administer such drug; or

(C) is limited by an effective application under section 505 to use under the professional supervision of a practitioner licensed by law to administer such drug,

shall be dispensed only (i) upon a written prescription of a practitioner licensed by law to administer such drug, or (ii) upon an oral prescription of such practitioner which is reduced promptly to writing and filed by the pharmacist, or (iii) by refilling any such written or oral prescription if such refilling is authorized by the prescriber either in the original prescription or by oral order which is reduced promptly to writing and filed by the pharmacist. The act of dispensing a drug contrary to the provisions of this paragraph shall be deemed to be an act which results in the drug being misbranded while held for sale.

(2) Any drug dispensed by filling or refilling a written or oral prescription of a practitioner licensed by law to administer such drug shall be exempt from the requirements of section 502, except paragraphs (a), (i) (2) and (3), (k), and (l), and the packaging requirements of paragraphs (g) and (h), if the drug bears a label containing the name and address of the dispenser, the serial number and date of the prescription or of its filling, the name of the prescriber, and, if stated in the prescription, the name of the patient, and the directions for use and cautionary statements, if any, contained in such prescription. This exemption shall not apply to any drug dispensed in the course of the conduct of a business of dispensing drugs pursuant to diagnosis by mail, or to a drug dispensed in violation of paragraph (1) of this subsection.

(3) The Administrator may by regulation remove drugs subject to section 502 (d) and section 505 from the requirements of paragraph (1) of this subsection when such requirements are not necessary for the production of the public health.

(4) A drug which is subject to paragraph (1) of this subsection shall be deemed to be misbranded if at any time prior to dispensing its label fails to bear the statement "Caution: Federal law prohibits dispensing without prescription". A drug to which paragraph (1) of this subsection does not apply shall be deemed to be misbranded if at any time prior to dispensing its label bears the caution statement quoted in the preceding sentence.

(5) Nothing in this subsection shall be construed to relieve any person from any requirement prescribed by or under authority of law with respect to drugs now included or which may hereafter be included within the classifications stated in section 8220 of the Internal Revenue Code (26 U. S. C. 3220), or to marihuana as defined in section 3238 (b) of the Internal Revenue Code (26 U. S. C. 3238 (b)).

C

EXCERPTS FROM UNITED STATES PHARMACOPEIA, NATIONAL FORMULARY AND FOOD AND NUTRITION BOARD, PUBLICATION

when there is a breakdown in homeostatic mechanisms or when the load of sodium presented to the body, or the losses issuing therefrom, exceeds the coping abilities of these mechanisms. Abnormal losses occur as a result of diarrhea and vomiting, in chronic renal disease, in adrenal insufficiency, and following the prolonged use of diuretics. Sweat contains 20 to 50 meq of sodium per liter, so that excessive sweating can lead to losses of as much as 350 meq of sodium per day. Whenever more than 4 liters of water are consumed, extra sodium chloride should be provided—approximately 17 mM (1 g) per liter of extra water. In unadapted individuals, the need for additional water may be somewhat higher. Sodium concentrations in sweat are high (50 to 150 meq/liter) in patients with cystic fibrosis of the pancreas.[5]

Diets restricted in sodium are used in the treatment of a number of conditions, notably those involving cardiac failure and edema formation. Since prolonged feeding of high-salt diets to experimental animals leads to hypertension, the possibility that excessive intakes could be of etiologic significance in human hypertensive disease is of current interest.

Potassium also is widely distributed in foods, the usual intake being 50 to 150 meq/day.[6] Potassium deficiency is a well-defined syndrome that complicates many pathologic states. Care should be used to ensure an adequate intake of potassium during prolonged intravenous feeding, during recovery from severe diarrhea or diabetic acidosis, and in patients given diuretics. An intake of 1 to 3 meq/kg/day should be sufficient for this purpose. High levels of serum potassium also lead to toxicity, principally manifested by cardiac conduction defects and cardiac failure, so it is imperative to curtail drastically or even eliminate dietary potassium in patients with advanced renal failure.

Chloride is the most important anion in the maintenance of fluid and electrolyte balance.[7,8] The daily turnover in adults (intake–output) ranges between 85 and 250 meq.

WATER

Water is the most abundant body constituent, accounting for 1/2 to 3/4 (depending on age and body fat) of the body weight. It is the milieu for all chemical processes. Deficits or excesses of more than a few percent are incompatible with health.[1] The normal rate of turn-

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Assay—Using a suitable quantity of Vitamin A, accurately weighed, proceed as directed under *Vitamin A Assay*, page 914.
Packaging and storage—Preserve in tight containers, preferably under an atmosphere of an inert gas, protected from light.
Labeling—Label it to indicate the form in which the vitamin is present, and to indicate the presence of any antimicrobial agent, dispersant, antioxidant, or other added substance, and to indicate the vitamin A activity in terms of the equivalent amount of retinol, in mg. per g., and in U. S. P. Vitamin A Units.*

CATEGORY: Anti-xerophthalmic vitamin; also see *Decavitamin Capsules* and *Tablets*.

USUAL DOSE: Prophylactic, 1.5 mg. (5000 U. S. P. Vitamin A Units) once a day.
Therapeutic, 7.5 mg. (25,000 Units) once a day.

USUAL DOSE RANGE: Prophylactic, 1.2 to 2.4 mg. (4000 to 8000 Units) daily.
Therapeutic, 7.5 to 60 mg. (25,000 to 200,000 Units) daily.

Vitamin A Capsules

Vitamin A Capsules contain not less than 95.0 percent of the labeled amount of vitamin A.

Weight variation, page 950: meet the requirements for *Capsules*.
Other requirements—The contents of Capsules respond to the *Identification tests* and meet the requirements of the test for *Absorbance ratio* under *Vitamin A*, page 775.
Assay—Using not less than 5 Vitamin A Capsules, proceed as directed under *Vitamin A Assay*, page 914. Calculate the content of retinol ($C_{20}H_{30}O$) in mg. and in U. S. P. Vitamin A Units per Capsule.
Packaging and storage—Preserve in tight, light-resistant containers.
Labeling—Label Capsules to indicate the form in which the vitamin is present, and to indicate the vitamin A activity in terms of the equivalent amount of retinol in mg. and in U. S. P. Vitamin A Units per Capsule.
Capsules available—Capsules usually available contain the following amounts of vitamin A: 1.5, 7.5, 15, and 30 mg. (5000, 25,000, 50,000, and 100,000 U. S. P. Vitamin A Units).

CATEGORY and DOSE: See *Vitamin A*.

Warfarin, Sodium *page 675*
Warfarin, Sodium, for Injection *page 676*
Warfarin, Sodium, Tablets *page 677*

Water

H_2O 18.02

Description: Clear, colorless, odorless liquid.

* NOTE—One U. S. P. Vitamin A Unit is the specific biologic activity of 0.3 mcg. of the all-*trans* isomer of retinol.

Reaction—[NOTE—For this test, use indicator test solutions specified for pH determinations (see under *Test Solutions* in the section, *Reagents, Indicators, and Solutions*, page 952).] Add 2 drops of methyl red T.S. to 10 ml. of Water in a test tube: no pink or red color is produced. To another 10-ml. portion of Water in a test tube add 2 drops of phenolphthalein T.S.: no pink or red color is produced.

Heavy metals—Adjust 40 ml. of Water with diluted acetic acid to a pH of 3.0 to 4.0 (using short-range pH indicator paper), add 10 ml. of freshly prepared hydrogen sulfide T.S., and allow the liquid to stand for 10 minutes: the color of the liquid, when viewed downward over a white surface, is not darker than the color of a mixture of 40 ml. of the same Water with the same amount of diluted acetic acid as was added to the sample and 10 ml. of Purified Water (see page 779), matched color-comparison tubes being used for the comparison.

Zinc—To 50 ml. contained in a test tube add 3 drops of glacial acetic acid and 0.5 ml. of potassium ferrocyanide T.S.: the solution shows no more turbidity than that produced by 50 ml. of purified water in a similar test tube, treated in the same manner, and viewed downward over a dark surface.

Foreign volatile matter—When heated nearly to the boiling point and agitated, it evolves no odor.

Total solids—Evaporate 100 ml. on a steam bath to dryness, and dry the residue at 105° for 1 hour: not more than 100 mg. of residue remains (0.1 percent).

Bacteriological purity—It meets the United States Public Health Service regulations for potable water with respect to bacteriological purity.

CATEGORY: Pharmaceutic aid (solvent).

Water for Injection

Water for Injection is water purified by distillation. It contains no added substance.

Caution—Water for Injection is intended for use as a solvent for the preparation of parenteral solutions. For parenteral solutions that are prepared under aseptic conditions and are not sterilized by appropriate filtration or in the final container, first render the Water for Injection sterile and thereafter protect it from microbial contamination.

Description: Clear, colorless, odorless liquid.

Pyrogen—When previously rendered isotonic by the addition of 900 mg. of pyrogen-free sodium chloride for each 100 ml., it meets the requirements of the *Pyrogen Test*, page 886.

Other requirements—It meets the requirements of the other tests under *Purified Water*, page 779, with the exception of the test for *Bacteriological purity*.

Packaging and storage—Preserve in tight containers. It may be stored at a temperature below or above the range in which microbial growth occurs.

CATEGORY: Pharmaceutic aid (solvent).

Bacteriostatic Water for Injection

Bacteriostatic Water for Injection is sterile water for injection containing one or more suitable antimicrobial agents.

Note—Use Bacteriostatic Water for Injection with due regard for the compatibility of the antimicrobial agent or agents it contains with the particular medicinal substance that is to be dissolved or diluted.

ONLY COPY AVAILABLE

Acid value, page 905: not less than 196 and not more than 204, about 2 g., accurately weighed, being used.
Iodine value, page 905: not less than 85 and not more than 95.
Packaging and storage—Preserve in tight containers.

CATEGORY: Pharmaceutic aid (solvent).

Olive Oil

Olive Oil is the fixed oil obtained from the ripe fruit of *Olea europæa* Linné (Fam. *Oleaceæ*).

Description: Pale yellow, or light greenish yellow, oily liquid, having a slight, characteristic odor and taste, with a faintly acrid aftertaste.
Solubility: Slightly soluble in alcohol. Miscible with ether, with chloroform, and with carbon disulfide.
Specific gravity, page 943: not less than 0.910 and not more than 0.915.
Heavy metals, *Method II*, page 897: 10 parts per million.
Cottonseed oil—Mix 5 ml. in a test tube with 5 ml. of a mixture of equal volumes of amyl alcohol and a 1 in 100 solution of sulfur in carbon disulfide, warm the mixture carefully to expel the carbon disulfide, and immerse the test tube to one-third of its length in a boiling, saturated solution of sodium chloride for 2 hours: the mixture develops no reddish color.
Peanut oil—Saponify 10 g. by heating for 1 hour under a reflux condenser with 80 ml. of alcoholic potassium hydroxide solution (1 in 20). Add phenolphthalein T.S., neutralize with diluted acetic acid, and wash the solution into 120 ml. of boiling lead acetate T.S. contained in a conical flask. Boil the mixture for 1 minute, and cool by immersing the flask in cold water, rotating the contents occasionally to cause the precipitate to adhere to the walls of the flask. Decant the liquid, wash the precipitate with cold water to remove the excess lead acetate, and then wash with 90 percent (by volume) alcohol. Add 100 ml. of ether, stopper the flask well, and allow to stand until the precipitate is disintegrated. Connect the flask to a reflux condenser, boil for 5 minutes, cool to about 15°, and allow to stand overnight. Filter, and thoroughly wash the precipitate with ether. With the use of a jet of ether, transfer the precipitate to a 500-ml. separator, alternating the jet of ether with diluted hydrochloric acid at the end if any of the precipitate adheres to the filter paper. Add sufficient diluted hydrochloric acid to make the total acid layer measure about 100 ml., and add sufficient ether to make the ether layer measure about 100 ml. Shake the mixture vigorously for several minutes, allow the layers to separate, draw off the acid layer, and wash the ether once by shaking with 50 ml. of diluted hydrochloric acid and finally with several portions of water until the last washing is not acid to methyl orange T.S. Transfer the ether solution to a dry flask, evaporate the ether, add a small amount of dehydrated alcohol, and evaporate on a steam bath to dryness. Dissolve the residue of dry fatty acids by warming with 60 ml. of 90 percent (by volume) alcohol, slowly cool the solution to 15° while shaking frequently, and allow the solution to stand at 15° for 30 minutes: no crystals separate from the solution.
Sesame oil—Mix 10 ml. with 10 ml. of hydrochloric acid, add 0.1 ml. of a 1 in 50 solution of furfural in alcohol, and shake the mixture vigorously for 15 seconds: no pink to crimson color appears in the acid layer when the emulsion breaks. If any color appears in the acid layer, add 10 ml. of water, and again shake the mixture vigorously: in the absence of sesame oil any pink color is evanescent.
Teaseed oil—In a dry, 18- × 150-mm. test tube place 0.8 ml. of acetic anhydride, 1.5 ml. of chloroform, and 0.2 ml. of sulfuric acid, mix, and cool in a water bath to 25°. Add about 200 mg. of Olive Oil (about 7 drops), mix, and cool to 25°. If the solution is cloudy, add acetic anhydride, dropwise, shaking after each addition, until the solution suddenly clears. Allow the mixture to remain in the water bath for 5 minutes: it shows a green color by both reflected and transmitted light. Add 10 ml. of absolute ether, and mix by inverting the tube: the initial green color fades to a brownish gray. (Before the dilution with ether, the presence of *teaseed oil* will cause a brown color to appear by transmitted light, and after the dilution, a transient red color.)
Free fatty acids, page 905—The free fatty acids in 10 g. require for neutralization not more than 5 ml. of 0.1 *N* sodium hydroxide.
Iodine value, page 905: not less than 79 and not more than 88.

Solubility: Freely soluble in water, in saline T.S., and in dextrose solutions; insoluble in most organic solvents.
Other requirements—It complies with the pH, moisture content, specific rotation, potency, and other requirements of the F.D.A. concerning Sodium Cephalothin.
Packaging and storage—Preserve in tight containers.

CATEGORY: Antibacterial.
USUAL DOSE: Parenteral, the equivalent of 500 mg. to 1 gram of cephalothin four to six times a day.
USUAL DOSE RANGE: 2 to 8 grams daily.

Sterile Sodium Cephalothin

Sterile Sodium Cephalothin is sodium cephalothin suitable for parenteral use. It contains not less than 90.0 percent and not more than 115.0 percent of the labeled amount of $C_{16}H_{15}N_3NaO_6S_2$. It conforms to the regulations of the federal Food and Drug Administration concerning antibiotic drugs (see *Antibiotics*, page 791).

Other requirements—It conforms to the definition, *Description*, and *Solubility* statement under *Sodium Cephalothin*, page 614. It complies with the identification, pH, moisture content, specific rotation, pyrogen, sterility, potency, and other requirements of the F.D.A. concerning Sterile Sodium Cephalothin.
Packaging and storage—Preserve in *Containers for Sterile Solids*, as described under *Injections*, page 797.
Sizes available—It is usually available in the following amounts: 1 and 4 g.

CATEGORY and DOSE: See *Sodium Cephalothin*.

Sodium Chloride

NaCl 58.44

Sodium Chloride contains not less than 99.5 percent and not more than 100.5 percent of NaCl, calculated on the dried basis. It contains no added substance.

Description: Colorless, cubic crystals or white, crystalline powder. Has a saline taste.
Solubility: Freely soluble in water, and slightly more so in boiling water; soluble in glycerin; slightly soluble in alcohol.
Identification—A solution (1 in 20) responds to the tests for *Sodium*, page 893, and for *Chloride*, page 892.
Acidity or alkalinity—Dissolve 50 g. in 200 ml. of carbon dioxide–free water, and add 10 drops of bromothymol blue pH indicator. If the solution is yellow, it requires not more than 1.0 ml. of 0.02 *N* sodium hydroxide to produce a blue color. If the solution is blue or green, it requires not more than 2.0 ml. of 0.02 *N* hydrochloric acid to produce a yellow color.
Loss on drying, page 935—Dry it at 105° for 2 hours: it loses not more than 0.5 percent of its weight.
Iodide or bromide—Digest 2 g. of finely powdered Sodium Chloride for 3 hours with 25 ml. of warm alcohol, cool the mixture, and remove the undissolved salt by filtration. Evaporate the filtrate to dryness, dissolve the residue in 5 ml. of water, add 1 ml. of chloroform, and cautiously introduce, dropwise, with constant agitation, 5 drops of dilute chlorine T.S. (1 in 3): the chloroform does not acquire a violet, yellow, or orange color.

Calcium and magnesium—Dissolve 20 g. in 200 ml. of water, add 0.1 ml. of hydrochloric acid, 5 ml. of a pH 10 buffer solution, and 5 drops of eriochrome black T.S. Titrate with 0.05 *M* disodium ethylenediaminetetraacetate to a pure blue end-point. Each ml. of 0.05 *M* disodium ethylenediaminetetraacetate is equivalent to 2.004 mg. of Ca. Not more than 0.05 percent of calcium and magnesium (as Ca) is found.

Sulfate, page 895—A 6.25-g. portion shows no more sulfate than corresponds to 0.15 ml. of 0.02 *N* sulfuric acid (150 parts per million).

Sodium ferrocyanide—Dissolve 25 g. in 80 ml. of water in a glass-stoppered, 100-ml. graduated cylinder or flask. Add 2 ml. of ferrous sulfate T.S. and 1 ml. of diluted sulfuric acid, dilute with water to 100 ml., and mix. For a control, dissolve another 25 g. in 80 ml. of water, dilute with water to 100 ml., and mix. Transfer 50-ml. portions of the respective solutions to matched color-comparison tubes: the solution to which ferrous sulfate T.S. was added shows no blue color when compared with the control.

Assay—Weigh accurately about 250 mg. of Sodium Chloride, dissolve in 50 ml. of water in a glass-stoppered flask, and add 50.0 ml. of 0.1 *N* silver nitrate, 3 ml. of nitric acid, 5 ml. of nitrobenzene, and 2 ml. of ferric ammonium sulfate T.S. Shake well, and titrate the excess silver nitrate with 0.1 *N* ammonium thiocyanate. Each ml. of 0.1 *N* silver nitrate is equivalent to 5.844 mg. of NaCl.

Packaging and storage—Preserve in well-closed containers.

CATEGORY: Electrolyte replenisher; also see *Dextrose and Sodium Chloride Injection*, *Mannitol and Sodium Chloride Injection*, *Ringer's Injection*, and *Lactated Ringer's Injection*.

USUAL DOSE: Oral, 1 gram three times a day.
Intravenous infusion, 1 liter of a 0.9 percent solution.
Topically to wounds and body cavities, as a 0.9 percent solution for irrigation.

USUAL DOSE RANGE: Oral, 3 to 6 grams daily.

Sodium Chloride Injection

Sodium Chloride Injection is a sterile, isotonic solution of sodium chloride in water for injection. It contains no antimicrobial agents. It contains not less than 0.85 percent and not more than 0.95 percent of NaCl.

Identification—It responds to the tests for *Sodium*, page 893, and for *Chloride*, page 892.

Pyrogen—It meets the requirements of the *Pyrogen Test*, page 886.

pH, page 938: between 4.5 and 7.0.

Arsenic, page 894—Use 35 ml. of Injection. The limit is 0.08 part per million.

Heavy metals, page 897—To 20 ml. of Injection add 2 ml. of diluted acetic acid, then dilute with water to 25 ml.: the heavy metals limit is 0.3 part per million.

Other requirements—It meets the requirements of the test for *Ferrocyanide* under *Dextrose and Sodium Chloride Injection*, page 181, except that 40 ml. of Injection is used, and it meets the requirements under *Injections*, page 797.

Assay—Pipet 25 ml. of Sodium Chloride Injection into a glass-stoppered flask, add 50 ml. of water, mix, and add 50.0 ml. of 0.1 *N* silver nitrate, 3 ml. of nitric acid, 5 ml. of nitrobenzene, and 2 ml. of ferric ammonium sulfate T.S. Shake well, and titrate the excess silver nitrate with 0.1 *N* ammonium thiocyanate. Each ml. of 0.1 *N* silver nitrate is equivalent to 5.844 mg. of NaCl.

Packaging and storage—Preserve in single-dose containers, preferably of Type I or Type II glass.

Injections available—Injection is usually available in the following volumes: 100, 150, 250, 500, and 1000 ml.

CATEGORY: Fluid and electrolyte replenisher; irrigating solution.

USUAL DOSE: Intravenous infusion, 1 liter.
Topically to wounds and body cavities, for irrigation.

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(*The United States Pharmacopeia*)

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radioisotopes it is therefore necessary to make the comparison of the spectrum with that of a known sample of the radionuclide obtained in the same instrument under identical conditions.

Radiation Shielding— Adequate shielding must be used to protect laboratory personnel from all ionizing radiation, and measuring instruments from background radiation.

Alpha and beta radiation is readily shielded because of its limited range of penetration. The range of alpha and beta particles varies inherently with their kinetic energy. The alpha particles are monoenergetic and have a range of a few centimeters in air. The absorption of beta particles, owing to their continuous energy spectrum and scattering, follows apparently an exponential function. The range of beta particles in air varies from centimeters to meters. Beta radiation produces an undesirable secondary radiation upon absorption by shielding materials. This radiation, known as Bremsstrahlung, resembles soft X-rays in its property of penetration. The higher the atomic number or density of the absorbing material, the greater the energy of the Bremsstrahlung produced. Elements of low atomic number produce low-energy Bremsstrahlung, which is readily absorbed; therefore, materials of low atomic number or of low density, such as aluminum, glass, or transparent plastic, are used to shield sources of beta radiation.

Gamma-ray radiation is deeply penetrating. Attenuation of gamma-ray radiation in matter is exponential and usually is expressed in terms of half-value layers. The half-value layer is the thickness of shielding material necessary to decrease the intensity of radiation to half its initial value. A shield of seven half-value thicknesses will reduce the radiation to less than 1 percent of its unshielded intensity of activity. Gamma-ray radiation is commonly shielded with lead.

Intensity of radiation is diminished according to the inverse square of the intervening distance between the source and the point of reference. Radioactive materials of multimillicurie strength can be handled safely in the laboratory by use of proper shielding and/or by arranging for the maximum practicable distance between the source and the operator by means of remote handling devices.

U. S. P. Reference Standards

Reference Standards are called for in many pharmacopeial assays and tests. Originally introduced for the biological assays of U. S. P. X, the use of reference standards has been extended to the point where they are now required for numerous other pharmacopeial assays as well. Some standards formerly required are still being distributed as a service to pharmacy and medicine for use as needed in unofficial assays.

On occasion, as a possible first step in pharmacopeial standardization, a reference standard or substance is provided as a standardized source of endocrine or enzyme activity in advance of the actual pharmacopeial recognition of a product representing that activity. In these cases, the articles supplied are designated as "substances" if they are heterogeneous in nature and if the prospect of their assuming pharmacopeial status is fairly remote; however, heterogeneous substances may be designated as "reference standards" if they are the counterparts of international standards.

The U. S. P. Reference Standards and U. S. P. Reference Substances are released under the authority of the U. S. P. Board of Trustees upon recommendation by the U. S. P. Reference Standards Committee, which supervises the testing and finally passes upon the suitability of each lot. The critical characteristics of the specimens selected for the standard are usually determined independently in three or more laboratories. At the request of the U. S. P. Reference Standards Committee, the Drug Standards Laboratory (see *Preface*) and the Food and Drug Administration laboratory test almost all new Standards and replacements for existing Standards. In addition, laboratories throughout the nation, both academic and industrial, participate in the testing.

A similar program to provide international standards is maintained by the World Health Organization, an agency of the United Nations. The WHO program is concerned mainly with standards for serums, toxins, vaccines, endocrine extracts, and vitamins. As a rule, an International Standard is no longer provided once the substance responsible for its characteristic activity has been isolated, identified, and

made readily available. A limited number of such compounds are distributed under WHO sponsorship as Authentic Chemical Substances for use in assays and tests of drugs. The U. S. P. Reference Standards Committee collaborates closely with the WHO in order not only to minimize unavoidable differences in the actual units of potency but also in some cases to share in the preparation of a reference standard.

No radioactive U. S. P. Reference Standards are provided, because of the special circumstances surrounding the preparation, storage, and distribution of standardized forms of radioactive substances suitable for use in drug analyses, despite the fact that some are called for in pharmacopeial assays and tests. Reliable standards of some radioactive substances, including chromium 51, cobalt 60, gold 198, iodine 131, and phosphorus 32, are available upon order from commercial sources.

Reference Standards are not available for substances subject to the licensing provisions established for narcotics.

The following U. S. P. Reference Standards are available (the Melting Point Standards are shown in *italics*, where listed individually).

Acetanilid
Acetazolamide
Allopurinol
Amitriptyline Hydrochloride
Amobarbital
Amphotericin B
Ampicillin
Ascorbic Acid
Aspirin
Atropine Sulfate
Benzalkonium Chloride
Benzathine Penicillin G
Gamma Benzene Hexachloride
Benztropine Mesylate
Betazole Hydrochloride
Bishydroxycoumarin
Caffeine
Calcium Disodium Edetate
Calcium Pantothenate
Carbachol
Chlorambucil
Chloramphenicol
Chlordiazepoxide Hydrochloride
Chlorobenzenes
Chloroquine Phosphate
Chlorpheniramine Maleate
Chlorpromazine Hydrochloride
Chlorpropamide
Chlorthalidone
Cholecalciferol[1]
Cholestyramine Resin
Corticotropin
Cortisone Acetate
Cyanocobalamin
Cyclizine Hydrochloride
Cyclophosphamide
Cycloserine
Demecarium Bromide
Desipramine
Desoxycorticosterone Acetate
Dexamethasone
Dexamethasone Phosphate
Dextroamphetamine Sulfate
Diaminodiphenylsulfone
Dibucaine Hydrochloride
Dichlorphenamide
Diethylstilbestrol
Diethyltoluamide
Digitalis
Digitoxin
Digoxin
Dihydrostreptomycin Sulfate
Dihydrotachysterol
Dioctyl Sodium Sulfosuccinate
Diphenhydramine Hydrochloride
Diphenylhydantoin
Disodium Edetate
Dyclonine Hydrochloride
Edrophonium Chloride
Epinephrine Bitartrate
Equilin
Ergocalciferol[2]
Ergonovine Maleate
Erythromycin
Erythromycin Ethylcarbonate
Erythromycin Gluceptate[3]
Erythromycin Lactobionate
Estradiol Valerate
Estrone
Ethacrynic Acid
Ethinyl Estradiol
Ethionamide
Ethosuximide
Ethoxzolamide
Ethynodiol Diacetate
Evans Blue
Fluorouracil
Fluoxymesterone
Folic Acid
Furosemide
Gallamine Triethiodide
Gentamicin Sulfate
Globin
Glucagon
Chorionic Gonadotropin
Griseofulvin
Guanethidine Sulfate
Hexachlorophene
Histamine Dihydrochloride
Homatropine Hydrobromide
Hydrochlorothiazide
Hydrocortisone
Hydrocortisone Acetate
Hydrocortisone Sodium Phosphate
Hydrocortisone Sodium Succinate

[1] Formerly called Activated 7-Dehydrocholesterol.

[2] Formerly called Calciferol.

[3] Formerly called Erythromycin Glucoheptonate.

Hydroxychloroquine Sulfate
Hydroxyprogesterone Caproate
Hydroxystilbamidine Isethionate
Idoxuridine
Imipramine Hydrochloride
Indocyanine Green
Insulin
Iodipamide
Iodochlorhydroxyquin
Iothalamic Acid
Isoproterenol Hydrochloride
Kanamycin Sulfate
Levallorphan Tartrate
Levarterenol Bitartrate
Lincomycin Hydrochloride
Liothyronine
Lucanthone Hydrochloride
Mecamylamine Hydrochloride
Meclizine Hydrochloride
Medroxyprogesterone Acetate
Melphalan
Melting Point Standards
Meprobamate
Mercaptopurine
Mestranol
Metaraminol Bitartrate
Methamphetamine Hydrochloride
Methazolamide
Methimazole
Methotrexate Reference Substance
Methyldopa
Methyldopate Hydrochloride
Methylene Blue
Methylergonovine Maleate
Methylphenidate Hydrochloride
Metyrapone
Neomycin Sulfate
Neostigmine Bromide
Neostigmine Methylsulfate
Niacinamide
Nitrofurantoin
Norethindrone
Norethynodrel
Novobiocin
Nystatin
Ouabain
Oxytetracycline
Oxytetracycline Hydrochloride
Phenacetin
Phenactin
Phenformin Hydrochloride
Phenobarbital
Phenolsulfonphthalein
Phenoxymethyl Penicillin
Phentolamine Mesylate[4]
Phenylephrine Hydrochloride
Physostigmine Salicylate
Phytonadione
Pilocarpine Nitrate
Posterior Pituitary
Negative Control Plastic
Polymyxin B Sulfate
Pralidoxime Chloride
Prednisolone
Prednisolone Acetate
Prednisone
Primidone
Probenecid
Procaine Hydrochloride
Prochlorperazine Maleate
Promethazine Hydrochloride
Proparacaine Hydrochloride
Propoxyphene Hydrochloride
Protamine
Pyrazinamide
Pyridostigmine Bromide
Pyridoxine Hydrochloride
Pyrimethamine
Pyrvinium Pamoate
Quinacrine Hydrochloride
Quinethazone
Quinidine Gluconate
Reserpine
Resorcinol
Riboflavin
Scopolamine Hydrobromide
Secobarbital
Sodium Ampicillin
Sodium Cephalothin
Sodium Cloxacillin
Sodium Colistimethate
Sodium Diatrizoate
Sodium Heparin[5]
Sodium Methicillin
Sodium Nafcillin
Sodium Oxacillin
Sodium Penicillin G
Sodium Sulfobromophthalein
Spironolactone
Streptomycin Sulfate
Sulfadiazine
Sulfamerazine
Sulfamethazine
Sulfanilamide
Sulfanilamide
Sulfapyridine
Sulfisoxazole
Testosterone Cypionate[6]
Testosterone Enanthate
Testosterone Propionate
Tetracaine Hydrochloride
Tetracycline Hydrochloride
Theophylline
Thiabendazole
Thiamine Hydrochloride
Thiopental
Thioridazine Hydrochloride
Thiotepa
Tolazamide
Tolbutamide
Tolnaftate
Triamcinolone
Triamcinolone Acetonide
Triamterene
Trihexyphenidyl Hydrochloride

[4] Formerly called Phentolamine Methanesulfonate.

[5] Formerly called Heparin Sodium.

[6] Formerly called Testosterone Cyclopentylpropionate.

Trimethaphan Camsylate
Tripelennamine Citrate
Tripelennamine Hydrochloride
Tropicamide
Tubocurarine Chloride
Vancomycin Hydrochloride
Vanillin
Vanillin
Vinblastine Sulfate
Vincristine Sulfate
Viomycin Sulfate
Vitamin A
Vitamin D Capsules
Vitamin D Oil
Warfarin
Zinc Bacitracin

Reference Standards and Reference Substances are available on a self-sustaining basis through orders addressed to: U. S. P. Reference Standards, 4630 Montgomery Ave., Bethesda, Md. 20014.

Spectrophotometry, Colorimetry, Turbidimetry, Nephelometry, and Fluorometry

Absorption spectrophotometry is the measurement of the absorption, by substances, of electromagnetic radiation of definite and narrow wavelength range, approximating monochromatic radiation. *Colorimetry* is the commonly accepted term for the measurement of light absorption, usually in the visible spectrum. *Turbidimetry* involves measurement of the degree of attenuation of a light beam incident on particles suspended in a medium, the measurement being made in the directly transmitted beam. *Nephelometry* involves measurement of the light scattered by suspended particles, the measurement usually being made perpendicularly to the incident beam. *Fluorometry* is the measurement of fluorescence, the light or other radiation emitted from a substance while it is being exposed to radiant energy.

The wavelength range available for these measurements extends from the short wavelengths of the ultraviolet through the infrared. For convenience of reference, this spectral range is roughly divided into the ultraviolet (185 mμ to 380 mμ), the visible (380 mμ to 780 mμ), the near-infrared (780 mμ to 3000 mμ), and the infrared (3 μ to 40 μ).

Comparative Utility of Spectral Ranges—For many pharmaceutical substances, measurements can be made in the ultraviolet and visible regions of the spectrum with greater accuracy and sensitivity than in the near-infrared and infrared. When solutions are observed in 1-cm. cells, concentrations of about 10 mcg. of the sample per ml. often will produce absorbances of 0.2 to 0.8. In the infrared and near-infrared, concentrations of 1 to 10 mg. per ml. and up to 100 mg. per ml., respectively, may be needed to produce sufficient absorption: for these spectral ranges, cell lengths of from 0.01 mm. to upwards of 3 mm. are commonly used.

The ultraviolet and visible spectra of a substance generally do not have as high a degree of selectivity as the infrared spectrum. Nevertheless, for many substances they are a useful means of identification and quantitative assay.

The infrared spectrum is usually unique for any given chemical compound with the exception of optical isomers, which have identical spectra. However, polymorphism may occasionally give rise to important differences in the infrared spectrum of a given compound in the solid state. Frequently, small differences in structure result in significant differences in spectra. Because of the large number of absorption bands in an infrared absorption spectrum, it is sometimes possible to measure quantitatively the individual components of a mixture of known qualitative composition without prior separation.

Theory and Terms—The power of a radiant beam decreases in relation to the distance that it travels through an absorbing medium. It also decreases in relation to the concentration of absorbing molecules or ions encountered in that medium. These two factors determine the proportion of the total incident energy that emerges in a relationship known as Beer's law.

The following definitions of spectrophotometric terms and symbols are here designated for pharmacopeial purposes:

Absorbance [Symbol: A]—The logarithm, to the base 10, of the reciprocal of the transmittance (T). (NOTE—Descriptive terms used formerly include optical density; absorbancy; and extinction.)

Absorptivity [Symbol: a]—The quotient of the absorbance (A) divided by the product of the concentration, expressed in *g.* per liter, of the substance and the absorption path length in cm. (NOTE—It is not to be confused with absorbancy index; specific extinction; or extinction coefficient.)

Molar Absorptivity [Symbol: ϵ]—The quotient of the absorbance (A) divided by the product of the concentration, expressed in *moles* per liter, of the substance and the absorption path length in cm. It is also

connected in series by means of glass and inert plastic tubing and suitable stoppers of glass, polymer, or cork (avoiding all use of rubber). Use one tube for the blank and the other for the sample. Arrange a gas-dispersion tube so that the hydrogen issues as bubbles at the bottom of each tube. Pass the hydrogen first through the blank tube and then through the sample tube.

Procedure—Pipet into a suitable vessel 25 ml. of the washed ether solution of the unsaponifiable fraction obtained as directed for *When Tocopherol Is Present* under *Procedure* in the *Vitamin A Assay*, page 914, and evaporate to about 5 ml. *Without applying heat*, remove the remaining ether in a stream of inert gas or by vacuum. Dissolve the residue in sufficient alcohol to give an expected concentration of about 0.15 mg. of alpha tocopherol per ml. Pipet 15 ml. into a 50-ml. centrifuge tube, add approximately 200 mg. of palladium catalyst, stir with a glass rod, and hydrogenate for 10 minutes in the *Hydrogenator*, using hydrogen that has been passed through alcohol in a blank tube. Add about 300 mg. of chromatographic siliceous earth, stir with a glass rod, and immediately centrifuge until the solution is clear.

Test a 1-ml. aliquot of the solution by removing the solvent by evaporation, dissolving the residue in 1 ml. of chloroform, and adding 10 ml. of antimony trichloride T.S.: no detectable blue color appears. [NOTE—If a blue color appears, repeat the hydrogenation for a longer time period, or with a new lot of catalyst.]

Pipet 2 ml. of the supernatant solution into a glass-stoppered, opaque flask, add 1.0 ml. of a 1 in 500 solution of ferric chloride in dehydrated alcohol,* and begin timing the reaction, preferably with a stop watch. Add immediately 1.0 ml. of a 1 in 200 solution of 2,2′-bipyridine in dehydrated alcohol, mix with swirling, add 21.0 ml. of dehydrated alcohol, close the tube, and shake vigorously to ensure complete mixing. When about 90 minutes has elapsed from the beginning of the reaction, transfer part of the mixture to one of a pair of matched 1-cm. spectrophotometer cells. After 10 minutes, accurately timed, following the addition of the ferric chloride-dehydrated alcohol solution, determine the absorbance at 520 mμ, with a suitable spectrophotometer, against dehydrated alcohol as the blank. Perform a blank determination with the same quantities of the same reagents and in the same manner, but using 2 ml. of dehydrated alcohol in place of the 2 ml. of the hydrogenated solution. Subtract the absorbance determined for the blank from that determined for the sample, and designate the difference as A_D.

Calculate the alpha tocopherol content, in mg., in the sample taken by the formula $30.24 A_D/(LC_D)$, in which A_D is the corrected absorbance, L is the length, in cm., of the absorption cell, and C_D is the content of the sample in the alcohol solution employed for the measurement of absorbance, expressed as g., capsules, or tablets per 100 ml.

* NOTE—The absorbance of the blank sometimes can be reduced, and the precision of the determination thereby improved, by purification of the dehydrated alcohol that is used throughout the assay. Purification may be accomplished by the addition of a few crystals (about 0.02 percent) of potassium permanganate and of a few pellets of potassium hydroxide to the dehydrated alcohol, and subsequent redistillation.

Vitamin A Assay

The following procedure is provided for the determination of vitamin A as an ingredient of Pharmacopeial preparations. It conforms to that which was adopted in 1956 for international use by the International Union of Pure and Applied Chemistry.

Complete the assay promptly, and exercise care throughout the procedure to keep to a minimum the exposure to actinic light and to atmospheric oxygen and other oxidizing agents, preferably by the use of non-actinic glassware and an atmosphere of an inert gas.

Special Reagents—

ETHER—Use *Ether*, page 249, freshly redistilled, discarding the first and last 10-percent portions.

Procedure—Accurately weigh, count, or measure a portion of the sample expected to contain the equivalent of not less than 0.15 mg. of retinol but containing not more than 1 g. of fat. If in the form of capsules, tablets, or other solid, reflux the portion taken in 10 ml. of water on a steam bath for about 10 minutes, crush the remaining solid with a blunt glass rod, and warm for about 5 minutes longer.

Transfer to a saponification flask,* and add 30 ml. of alcohol if the sample is liquid or 23 ml. of alcohol and 7 ml. of glycerin if the sample is solid, followed by 3 ml. of potassium hydroxide solution (9 in 10). Reflux in an *all-glass* apparatus for 30 minutes. Cool the solution, add 30 ml. of water, and transfer to a conical separator. Add 2 g. of finely powdered sodium sulfate. Extract by shaking for 2 minutes with one 150-ml. portion of ether, and, if an emulsion forms, with three additional 25-ml. portions

of ether. Combine the ether extracts, if necessary, and wash by swirling gently with 50 ml. of water. Repeat the washing more vigorously with three additional 50-ml. portions of water. Transfer the washed ether extract to a 250-ml. volumetric flask, and add ether to volume.

Evaporate a 25.0-ml. portion of the ether extract to about 5 ml. *Without applying heat and with the aid of a stream of inert gas or vacuum,* continue the evaporation to about 3 ml. Dissolve the residue in sufficient isopropyl alcohol to give an expected concentration of the equivalent of 3 to 5 mcg. of vitamin A per ml. or such that it will give an absorbance in the range 0.5 to 0.8 at 325 mμ. Determine the absorbances of the resulting solution at the wavelengths 310 mμ, 325 mμ, and 334 mμ, with a suitable spectrophotometer fitted with matched quartz cells.

WHEN TOCOPHEROL IS PRESENT—Transfer to a saponification flask a suitable sample, accurately measured, or not less than 5 previously crushed Decavitamin Capsules or Decavitamin Tablets. Reflux in an *all-glass* apparatus with 30 ml. of alcohol and 3 ml. of potassium hydroxide solution (9 in 10) for 30 minutes. Add through the condenser 2.0 g. of hydrous citric acid, washing the walls of the condenser with 10 ml. of water. Cool, and transfer the solution to a conical separator with the aid of 20 ml. of water. Add 2 g. of finely powdered sodium sulfate. Extract with one 150-ml. portion of ether, and, if an emulsion forms, with three additional 25-ml. portions of ether. Combine the ether extracts, if necessary, and wash by swirling gently with 50 ml. of water. Repeat the washing more vigorously with three additional 50-ml. portions of water. Transfer the washed ether extract to a 250-ml. volumetric flask, and add ether to volume. Transfer a 100.0-ml. aliquot of the resulting ether solution to a conical separator, and wash once with 50 ml. of potassium hydroxide solution (1 in 33), using alcohol, if necessary, to break any emulsion that forms. Wash by swirling gently with 50 ml. of water. Repeat the washing more vigorously with three additional 50-ml. portions of water. Transfer the washed ether extract to a 100-ml. volumetric flask, and add ether to volume.

Evaporate a 50.0-ml. aliquot of the ether solution of the unsaponifiable extract to about 5 ml. *Without applying heat and with the aid of a stream of inert gas or vacuum,* remove the residual ether. Dissolve the residue in 50.0 ml. of isopropyl alcohol.

Hydrogenated portion—Pipet 15 ml. of the isopropyl alcohol solution into a 50-ml. centrifuge tube, add approximately 200 mg. of palladium catalyst, stir with a glass rod, and hydrogenate for 10 minutes in a *Hydrogenator* such as is described in the *Alpha-Tocopherol Assay*, page 913, using isopropyl alcohol in the blank tube. Add about 500 mg. of chromatographic siliceous earth, stir with a glass rod, and immediately centrifuge until the solution is clear.

Test a 1-ml. aliquot of the solution by removing the solvent by evaporation, dissolving the residue in 1 ml. of chloroform, and adding 10 ml. of antimony trichloride T.S.: no detectable blue color appears. [NOTE—If a blue color appears, repeat the hydrogenation for a longer time period, or with a new lot of catalyst.]

Into two separate flasks pipet equal volumes of the *Hydrogenated portion* and the untreated isopropyl alcohol solution, respectively, and add sufficient isopropyl alcohol to give an expected concentration of vitamin A equivalent to 3 mcg. to 5 mcg. per ml. Determine the absorbances of the untreated solution against the solution from the *Hydrogenated portion* as a blank, at the wavelengths 310 mμ, 325 mμ, and 334 mμ, with a suitable spectrophotometer fitted with matched quartz cells.

Calculation—Calculate the vitamin A content as follows:

$$\text{Content (in mg.)} = 0.549A_{325}/LC,$$

in which A_{325} is the observed absorbance at 325 mμ, L is the length, in cm., of the absorption cell, and C is the amount of sample expressed as g., capsule, or tablet in each 100 ml. of the final isopropyl alcohol solution, provided that A_{325} has a value not less than $[A_{325}]/1.030$ and not more than $[A_{325}]/0.970$, where $[A_{325}]$ is the *corrected* absorbance at 325 mμ and is given by the equation $[A_{325}] = 6.815A_{325} - 2.555A_{310} - 4.260A_{334}$, in which A designates the absorbance at the wavelength indicated by the subscript.

Where $[A_{325}]$ has a value less than $A_{325}/1.030$, apply the following equation:

$$\text{Content (in mg.)} = 0.549[A_{325}]/LC,$$

in which the values are as defined herein.

Confidence Interval—The range of the limits of error, indicating the extent of discrepancy to be expected in the results of different laboratories at $P = 0.05$, is approximately ±8 percent.

Vitamin D Assay

The following procedure is provided for the determination of vitamin D as an ingredient of Pharmacopeial preparations.

Complete the assay promptly, and exercise care throughout the procedure to keep to a minimum the exposure to air and to

actinic light, preferably by the use of a blanket of inert gas and low-actinic glassware.

Special Reagents and Solutions—

CHROMATOGRAPHIC FULLER'S EARTH—Use chromatographic fuller's earth having a water content corresponding to not less than 8.5 percent and not more than 9.0 percent of loss on drying.

SOLVENT HEXANE—Use solvent hexane (see under *Reagents*), redistilling if necessary so that it meets the following additional specification:

Spectral purity—Measure in a 1-cm. cell at 300 mμ, with a suitable spectrophotometer, against air as the blank: the absorbance is not more than 0.070.

ETHYLENE DICHLORIDE—Purify by passage through a column of granular (20 to 200 mesh) silica gel.

POTASSIUM HYDROXIDE SOLUTION—Dissolve 500 g. of potassium hydroxide in water to make 1000 ml.

BUTYLATED HYDROXYTOLUENE SOLUTION—Dissolve 10 mg. of butylated hydroxytoluene in 100 ml. of alcohol. Prepare this solution fresh daily.

COLOR REAGENT—Prepare two stock solutions as follows.

Solution A—Empty, without weighing, the entire contents of a previously unopened 113-g. bottle of dry, crystalline antimony trichloride into a flask containing about 400 ml. of *Ethylene Dichloride*. Add about 2 g. of anhydrous alumina, mix, and filter through filter paper into a clear-glass, glass-stoppered container calibrated at 500 ml. Add *Ethylene Dichloride* to make 500 ml., and mix: the absorbance of the solution, measured in a 20-mm. cell at 500 mμ, with a suitable spectrophotometer, against *Ethylene Dichloride*, does not exceed 0.070.

Solution B—Mix, under a hood, 100 ml. of acetyl chloride and 400 ml. of *Ethylene Dichloride*.

Mix 45 ml. of *Solution A* and 5 ml. of *Solution B* to obtain the *Color Reagent*. Store in a tight container, and use within 7 days, but discard any reagent in which a color develops.

Chromatographic Tubes—

FIRST COLUMN—Arrange for descending column chromatography a tube of 2.5-cm. (inside) diameter, about 25 cm. long, and constricted to 8-mm. diameter for a distance of 5 cm. at the lower end, by inserting at the point of constriction a coarse-porosity, sintered-glass disk or a small plug of glass wool. The constricted portion may be fitted with an inert, plastic stopcock.

SECOND COLUMN—Select a tube that is made up of three sections: (1) a flared top section, 18 mm. in (inside) diameter and approximately 14 cm. long, (2) a middle section, 6 mm. in (inside) diameter and approximately 25 cm. long, and (3) a tapered, constricted lower exit tube approximately 5 cm. long. Insert a small plug of glass wool in the upper 1-cm. portion of the constricted section.

Chromatographic Columns—

FIRST COLUMN—To about 125 ml. of isooctane contained in a screw-capped, wide-mouth bottle add 25 g. of chromatographic siliceous earth, and shake until a slurry is formed. Add, dropwise and with vigorous mixing, 10 ml. of polyethylene glycol 600. Replace the bottle cover, and shake vigorously for 2 minutes. Pour about half of the resulting slurry into the chromatographic tube, and allow it to settle by gravity. Then apply gentle suction, and add the remainder of the slurry in small portions, packing each portion with a 20-mm. disk plunger. When a solid surface has formed, remove the vacuum, and add about 2 ml. of isooctane.

SECOND COLUMN—Pack the midsection of the tube with 3 g. of moderately coarse *Chromatographic Fuller's Earth* with the aid of gentle suction (about −125 mm. of mercury).

Standard Preparation—Dissolve about 25 mg. of U. S. P. Ergocalciferol Reference Standard, accurately weighed, in sufficient isooctane to give a known concentration of about 250 mcg. per ml. Store in a refrigerator.

On the day of assay, pipet 1 ml. of the standard solution into a 50-ml. volumetric flask, remove the solvent with a stream of nitrogen, and dissolve the residue in, and make to volume with, *Ethylene Dichloride*.

Sample Preparation—Accurately weigh or measure a portion of the sample to be assayed, equivalent to not less than 125 mcg. but preferably about 250 mcg. of ergocalciferol (10,000 U. S. P. Units). If little or no vitamin A is present in the sample, add about 1.5 mg. (the equivalent of 3000 U. S. P. Units) of vitamin A acetate to provide the needed pilot bands in the subsequent chromatography.

For capsules or tablets, reflux not less than 10 of them in 10 ml. of water on a steam bath for about 10 minutes, crush the remaining solid with a blunt glass rod, and warm for 5 minutes longer.

Add a volume of *Potassium Hydroxide Solution* representing 2.5 ml. for each g. of the total weight of the sample, but not less than a total of 3.0 ml. Add 10 ml. of *Butylated Hydroxytoluene Solution* and 20 ml. of alcohol. Reflux vigorously on a steam bath for 30 minutes. Cool, and transfer the saponified mixture to a conical separator, rinsing the saponification flask with three 10-ml. portions of water and three 50-ml. portions of ether, adding each rinse to the separator. Add about 4 g. of sodium sulfate decahydrate to the separator,

and extract by shaking for 2 minutes. If an emulsion forms, extract with three 25-ml. portions of ether. Combine the ether extracts, if necessary, and wash by swirling gently with 50 ml. of water. Repeat the washing more vigorously with additional 50-ml. portions of water until the last portion shows no pink color on the addition of phenolphthalein T.S. Transfer the washed ether extract to a 250-ml. volumetric flask, add ether to volume, and mix. Transfer the entire sample or an accurately measured aliquot containing about 250 mcg. to a tall-form, 400-ml. beaker containing about 5 g. of anhydrous sodium sulfate. Stir for 2 minutes, then decant the solution into a second 400-ml. beaker. Rinse the sodium sulfate with three 25-ml. portions of ether, adding each rinse to the main portion. Reduce the total volume to about 30 ml. by evaporation on a steam bath, and transfer the concentrate to a small, round-bottom evaporation flask. Rinse the beaker with three 10-ml. portions of ether, adding the rinsings to the flask. With the aid of vacuum in a water bath at a temperature not exceeding 40°, or with a stream of nitrogen at room temperature, remove the remaining solvent completely. Dissolve the residue in a small amount of *Solvent Hexane*, transfer to a 10-ml. volumetric flask, and dilute with *Solvent Hexane* to volume to obtain the *Sample Preparation*.

Procedure—

FIRST COLUMN CHROMATOGRAPHY—Just as the 2 ml. of isooctane disappears into the surface of the prepared *First Column*, pipet 2 ml. of the *Sample Preparation* onto the column. As the meniscus of the *Sample Preparation* reaches the column surface, add the first of three 2-ml. portions of *Solvent Hexane*, adding each succeeding portion as the preceding portion disappears into the column. Continue adding *Solvent Hexane* in portions of 5 to 10 ml. until 100 ml. has been added. If necessary, adjust the flow rate to between 3 and 6 ml. per minute, by application of gentle pressure at the top of the chromatographic tube.

Discard the first 20 ml. of effluent, and collect the remainder. Examine the column under ultraviolet light at intervals during the chromatography, and stop the flow when the front of the fluorescent band representing vitamin A is about 5 mm. from the bottom of the column. (The ultraviolet lamp should provide *weak* radiation in the 300-mμ region. It is frequently necessary to use a narrow aperture or screen with commercial lamps to reduce the amount of radiation to the minimum required to visualize the vitamin A on the column.)

Transfer the eluate to a suitable evaporation flask, and remove the solvent hexane completely under vacuum at a temperature not above 40° or with a stream of nitrogen at room temperature. Dissolve the residue in about 10 ml. of *Solvent Hexane*.

SECOND COLUMN CHROMATOGRAPHY—Add the solvent hexane solution obtained as directed under *First Column Chromatography* onto the *Second Column*. Rinse the evaporation flask with a total of 10 ml. of *Solvent Hexane* in small portions, adding each portion to the *Second Column* and allowing it to flow through the column, and discard the effluent. When about 1 ml. of the solvent hexane remains above the surface of the column, add 75 ml. of benzene, and elute with the aid of gentle suction (about −125 mm. of mercury), collecting the eluate. Evaporate the benzene under vacuum at a temperature not above 40°, or with a stream of nitrogen at room temperature.

ASSAY PREPARATION—Dissolve the residue obtained as directed under *Second Column Chromatography* in a small amount of *Ethylene Dichloride*, transfer to a 10-ml. volumetric flask, and make to volume with *Ethylene Dichloride* to obtain the *Assay Preparation*.

COLOR DEVELOPMENT—Into each of three suitable, matched colorimeter tubes of about 20-mm. (inside) diameter, and designated *1*, *2*, and *3*, respectively, pipet 1 ml. of the *Assay Preparation*. Into tube *1* pipet 1 ml. of the *Standard Preparation*, into tube *2*, 1 ml. of *Ethylene Dichloride*, and into tube *3*, 1 ml. of a mixture of equal volumes of acetic anhydride and *Ethylene Dichloride*. To each tube add quickly, and preferably from an automatic pipet, 5.0 ml. of *Color Reagent*, and mix. After 15 seconds, accurately timed, following the addition of the color reagent, determine the absorbances of the three solutions at 500 mμ, with a suitable spectrophotometer, using *Ethylene Dichloride* as the blank. Similarly, 45 seconds after making the first reading on each solution, determine the absorbances of the solutions in tubes *2* and *3* at 550 mμ, in a similar manner. Designate the absorbances as A^1_{500}, A^2_{500}, A^3_{500}, A^3_{550}, and A^3_{550}, respectively, in which the superscript indicates the number of the tube and the subscript the wavelength.

Calculation—Calculate the quantity, in mcg., of vitamin D in the portion of the sample taken by the formula $(C_S/C_U)(A_U/A_S)$, in which C_S is the concentration of vitamin D in mcg. per ml. of the *Standard Preparation*, C is the concentration of the sample (as g., capsules, tablets, etc.) in each ml. of the final solution, A_U has the value of $(A^1_{500} - A^2_{500}) - 0.67(A^3_{550} - A^3_{550})$ determined from the absorbances observed on the solution from the *Assay Preparation*, and A_S has the value of $A^1_{500} - A^2_{500}$ determined on the solution from the *Standard Preparation*.

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tions and conversion charts obtainable from the American Society for Testing and Materials.

Procedure for Cellulose Derivatives—Measurement of the viscosity of solutions of the high-viscosity types of cellulose derivatives is a special case, since they are too viscous for the commonly available viscosimeters. The Ubbelohde viscosimeter may be adapted as illustrated in the accompanying illustration (or ASTM, D-1347), to the measurement of the ranges of viscosity encountered in methylcellulose solutions.

Calibration of the Ostwald Type Viscosimeter—Determine the viscosimeter constant, k, for each viscosimeter by the use of an oil of known viscosity.† Place an excess of the oil (adjusted to 20 ± 0.1°) in the filling tube and transfer it to the orifice tube by gentle suction, taking care to prevent bubble formation in the liquid by keeping the air vent tube closed. Adjust the meniscus of the column of liquid in the orifice tube to the level of the top graduation line. Open both the vent and orifice tubes in order to permit the liquid to flow into the reservoir against atmospheric pressure. (Failure to open the vent tube before releasing the orifice tube will yield false values.) Record the time in seconds for the liquid to flow from the upper mark to the lower mark in the orifice tube.

Calculate the viscosimeter constant, k, from the equation $k = v/dt$, in which v is the known viscosity of the liquid in centipoises, d is the specific gravity of the liquid tested at 20°/20°, and t is the time in seconds for the liquid to pass from the upper mark to the lower mark.

If a viscosimeter is repaired, it must be recalibrated, since even minor repairs frequently cause significant changes in the value of its constant, k.

† Oils of known viscosities formerly supplied by the National Bureau of Standards, may be obtained from the Cannon Instrument Co., Post Office Box 16, State College, PA 16801. For methylcellulose, choose an oil the viscosity of which is as close as possible to that of the type of methylcellulose to be determined.

VITAMIN A ASSAY

Complete the assay promptly and exercise care throughout the procedure to avoid undue exposure to oxidizing agents, to actinic light, and to other conditions that destroy vitamin A. The use of nonactinic glassware is advantageous in avoiding destruction by light.

Isopropyl alcohol—Use *Isopropyl Alcohol*, distil, if necessary, to meet the following requirements for spectral purity: when measured in a 1-cm. cell against distilled water it shows an absorbance not greater than 0.05 at 300 mμ and not greater than 0.01 between 320 mμ and 350 mμ.

Ether—Use *Ether*, freshly distilled, discarding the first and last 10 percent portions, or *Ether*, anesthetic grade, from a freshly opened container.

Saponification—Transfer to a saponification flask an amount of the sample, accurately measured and expected to contain not less than the equivalent of 150 mcg. of vitamin A, but not more than 1 g. of fat: Reflux in an *all-glass* apparatus with 30 ml. of alcohol and 3 ml. of potassium hydroxide solution (1 in 2) for 30 minutes. Cool the solution, add 30 ml. of water, and transfer the resulting solution to a conical separator. Add 2 g. of finely powdered sodium sulfate. Extract, by shaking for 2 minutes, with one 150-ml. portion of ether, or, if an emulsion occurs, with three additional 25-ml. portions of ether. Combine the ether extracts, if necessary, and wash by swirling gently with 50 ml. of water. Repeat the washing more vigorously until the last washing gives no color with phenolphthalein T.S. Transfer the washed ether extract to a 250-ml. volumetric flask, and dilute to volume with ether.

Procedure—Evaporate a 25.0-ml. aliquot of the ether solution of the unsaponifiable extract to about 5 ml. Without the application of heat, reduce the volume to about 3 ml. in a stream of inert gas or under reduced pressure. Dissolve the residue in sufficient isopropyl alcohol to give an expected concentration of the equivalent of 3 to 5 mcg. of vitamin A per ml. or such that it will give an absorbance in the range 0.4 to 0.8 at 325 mμ. Determine the absorbances of the resulting solution in 1-cm. cells, at 310 mμ, 325 mμ, and 334 mμ with a suitable spectrophotometer, using isopropyl alcohol as the blank.

Calculation—Calculate the vitamin A content as follows: Vitamin A content (in mg.) = $0.549 \times (A_{325}/LC)$, in which A_{325} is the observed absorbance at 325 mμ, L is the length, in cm., of the absorption cell, and C is the amount of sample expressed as g., capsule or tablet, in each 100 ml. of the final isopropyl alcohol solution, provided that A_{325} has a value not less than $A_{325}(\text{cor.})/1.030$ and not more than $A_{325}(\text{cor.})/0.970$, where $A_{325}(\text{cor.}) = 6.815A_{325} - 2.555A_{310} - 4.260A_{334}$, in which A designates the absorbance at the wavelengths indicated by the subscripts. Where $A_{325}(\text{cor.})$ has a value less than $A_{325}/1.030$ apply the following formula: Vitamin A content, in mg., = $0.549[A_{325(\text{cor.})}/LC]$. Each mg. of vitamin A (alcohol)

represents 3333 USP Units of vitamin A.

Confidence Interval—The range of the limits of error, indicating the extent of discrepancy to be expected in the results of different laboratories at $P = 0.05$, is approximately ±8 percent.

VITAMIN B_{12} ACTIVITY ASSAY

Assay Preparation—Place a suitable quantity of the material to be assayed, accurately measured or weighed, in an appropriate vessel containing, for each g. or ml. of sample taken, 25 ml. of an aqueous extracting solution prepared just prior to use to contain, in each 100 ml., 1.29 g. of disodium phosphate, 1.1 g. of anhydrous citric acid, and 1.0 g. of sodium metabisulfite. Autoclave the mixture at 121° for 10 minutes. Allow any undissolved particles of the sample extract to settle, and filter or centrifuge if necessary. Dilute an aliquot of the clear solution with water so that the final test solution contains vitamin B_{12} activity approximately equivalent to that of the *Standard Cyanocobalamin Solution* which is added to the assay tubes.

Standard Cyanobalamin Stock Solution—To a suitable quantity of USP Cyanocobalamin Reference Standard, accurately weighed, add sufficient 25 percent alcohol to make a solution containing, in each ml., 1.0 mcg. of cyanocobalamin. Store in a refrigerator.

Standard Cyanocobalamin Solution—Dilute a suitable volume of *Standard Cyanocobalamin Stock Solution* with water to a measured volume such that after the incubation period as described under *Procedure*, the difference in transmittance between the inoculated blank and the 5.0-ml. level of the *Standard Cyanocobalamin Solution* is not less than that which corresponds to a difference of 1.25 mg. in dried cell weight. This concentration usually falls between 0.01 and 0.04 millimicrogram per ml. of *Standard Cyanocobalamin Solution*. Prepare a fresh standard solution for each assay.

Basal Medium Stock Solution—Add the ingredients in the order listed, carefully dissolving the cystine and tryptophane in the hydrochloric acid before adding the next eight solutions in the resulting solution. Add 100 ml. of water, mix, and dissolve the dextrose, sodium acetate, and ascorbic acid. Filter, if necessary, add the polysorbate 80 solution, adjust the reaction to pH 6.0 with 1 *N* sodium hydroxide, and add purified water to make 250 ml.

L-Cystine	0.1	g.
L-Tryptophane	0.05	g.
1 *N* Hydrochloric Acid	10	ml.
Adenine-Guanine-Uracil Solution	5	ml.
Xanthine Solution	5	ml.
Vitamin Solution I	10	ml.
Vitamin Solution II	10	ml.
Salt Solution A	5	ml.
Salt Solution B	5	ml.
Asparagine Solution	5	ml.
Acid-hydrolyzed Casein Solution	25	ml.
Dextrose, Anhydrous	10	g.
Sodium Acetate, Anhydrous	5	g.
Ascorbic Acid	1	g.
Polysorbate 80 Solution	5	ml.

Acid-hydrolyzed Casein Solution—Mix 100 g. of vitamin-free casein with 500 ml. of dilute hydrochloric acid (1 in 2), and reflux the mixture for 8 to 12 hours. Remove the hydrochloric acid from the mixture by distillation under reduced pressure until a thick paste remains. Redissolve the resulting paste in water, adjust the solution to a pH of 3.5 ± 0.1 with sodium hydroxide solution, and add water to make 1000 ml. Add 20 g. of activated charcoal, stir for 1 hour, and filter. Repeat the treatment with activated charcoal. Store under toluene in a refrigerator at a temperature not below 10°. Filter the solution if a precipitate forms under storage.

Asparagine Solution—Dissolve 2.0 g. of *L*-asparagine in water to make 200 ml. Store under toluene in a refrigerator.

Adenine-Guanine-Uracil Solution—Dissolve 200 mg. each of adenine sulfate, guanine hydrochloride, and uracil, with the aid of heat, in 10 ml. of dilute hydrochloric acid (1 in 3), cool, and add water to make 200 ml. Store under toluene in a refrigerator.

Xanthine Solution—Suspend 0.2 g. of xanthine in 30 to 40 ml. of water, heat to about 70°, add 6.0 ml. of ammonia T.S., and stir until the solid is dissolved. Cool, and add water to make 200 ml. Store under toluene in a refrigerator.

Salt Solution A—Dissolve 10 g. of monobasic potassium phosphate and 10 g. of dibasic potassium phosphate in water to make 200 ml. Add 2 drops of hydrochloric acid, and store under toluene.

Salt Solution B—Dissolve 4.0 g. of magnesium sulfate, 0.2 g. of sodium chloride, 0.2 g. of ferrous sulfate, and 0.2 g. of manganese sulfate in water to make 200 ml. Add 2 drops of hydrochloric acid, and store under toluene.

Polysorbate 80 Solution—Dissolve 20 g. of polysorbate 80 in sufficient alcohol to make 200 ml. Store in a refrigerator.

Vitamin Solution I—Dissolve 10 mg. of riboflavin, 10 mg. of thiamine hydrochloride, 0.1 mg. of biotin, and 20 mg. of nicotinic acid in sufficient 0.02 *N* acetic acid to

VITAMIN D ASSAY

Biological Method

The biological assay of vitamin D comprises the recording and interpretation of observations on groups of rats maintained on specified dietary regimens throughout specified periods of their lives whereby the biological response to the preparation under assay is compared with the response to USP Vitamin D Reference Standard.

Preliminary Period—Throughout the preliminary period in the life of a rat, which is not longer than 30 days and extends from birth to the first day of the depletion period, maintain litters of rats under the immediate supervision of, or according to the directions of, the individual responsible for the assay. During the preliminary period, use a dietary regimen which provides for normal development but is limited in its content of vitamin D, so that when placed upon the *Rachitogenic Diet* in the depletion period the rats develop rickets. At the end of the preliminary period, reject any rat which weighs less than 44 g. or more than 60 g., or which shows evidence of injury, disease, or anatomical abnormality.

Depletion Period—Through the depletion period, which extends from the end of the preliminary period to the first day of the assay period, provide each rat *ad libitum* with the *Rachitogenic Diet* and water and allow access to no other food or dietary supplement.

Rachitogenic Diet—The rachitogenic diet consists of a uniform mixture of the following ingredients in the proportions shown:

	Parts by Weight
Whole Yellow Corn, ground	76
Ground Wheat Gluten	20
Calcium Carbonate	3
Sodium Chloride	1

When a chemical analysis of the entire ration shows a Ca:P ratio of less than 4:1 or more than 5:1, the proportion of calcium carbonate may be varied to bring the adjusted ratio to a uniform level within this range.

Assigning Rats to Groups for the Assay Period—Consider a litter suitable for the assay period when individual rats in the litter show evidence of rickets such as enlarged joints and a distinctive wobbly, rachitic gait, provided that the depletion period is not less than 19 or more than 25 days. The presence of rickets may be established also from the width of the rachitic metaphysis upon X-ray examination or by applying the line test (described below) to a leg bone of one member of each litter.

Record the weight of each rat and assign it to a group, in which each rat will be fed a specified dose of the reference standard or of an assay sample that is under examination for its vitamin D potency. For each assay sample provide one or more assay groups and at least two standard groups. The two standard groups may be used for the concurrent assay of more than one assay sample. Within an interval not exceeding 30 days, complete the assignment of rats to groups according to a design which divides litters among the groups, to achieve a complete balance.

For complete balance, whereby each litter is represented equally in every group, use seven or more litters containing at least as many depleted rats as there are groups. From a given litter, assign one rat, selected at random, to each group on the same day. If a litter contains twice as many rats as there are groups, assign a second series of rats similarly. The last one or two litters to be assigned may be allotted to groups so that at the start of the assay period the average body weight of any completed groups will not differ by more than 8 g. from that of any other group.

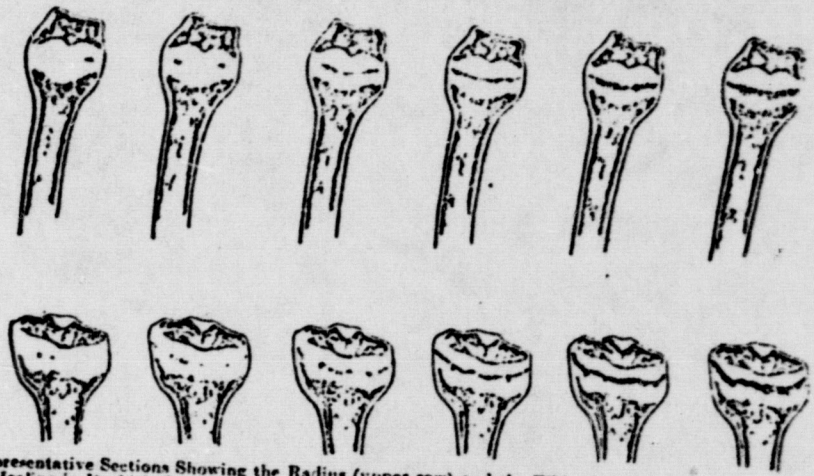
Assay Doses—Select two dosage levels of the USP Vitamin D Reference Standard, spaced so that the ratio of the larger to the smaller dose is not less than 1.5 or more than 2.5. Select one or two dosage levels based upon a single assumed potency for each sample. The dosage levels of the sample are equivalent to those of the standard or to a mid-level equal to the square root of the product of the two dosage levels of the standard.

Select dosage levels such that, when fed to rachitic rats, they are expected to produce degrees of calcification within the range specified under the test of data acceptability. Before feeding, the reference standard and/or sample may be diluted with cottonseed oil, provided that not more than 0.2 ml. is fed on any one day. Store the oil solutions in well-closed bottles, protected from light, at a temperature not exceeding 10°, and use within 5 weeks.

Assign one group of rats to each dosage level of the standard and of the one or more samples.

Assay Period—During the assay period, which extends from the end of the depletion period for a fixed interval of 7 to 10 days, cage each rat individually and provide it *ad libitum* with the *Rachitogenic Diet* and water. Supply a rachitogenic diet prepared from the same lots of ingredients to all rats. On the first and on the third (or fourth) day of the assay period, feed each rat one-half of its total assigned dose.

Throughout the assay period, maintain as uniform environmental conditions as possible for all rats and exclude exposure to



Representative Sections Showing the Radius (upper row) and the Tibia (lower row) in Graded Degrees of Healing in Rachitic Rats within the Useful Range of the Dosage-Response Relationship of the Vitamin D Assay

antirachitic radiations. At the end of a fixed period of 7 to 10 days, weigh and kill each rat. From those rats which do not weigh less at the end than at the start of the assay period and which have consumed each assigned dose within 24 hours of the time it was fed, dissect out one or more leg bones for examination by the *Line Test*.

Line Test—Remove the proximal end of a tibia or the distal end of a radius and clean it of adhering tissue, in any one assay using the same bone from all animals. With a clean, sharp blade cut a median, longitudinal section through the juncture of the epiphysis and diaphysis at the same place on each bone. Rinse both sections in purified water, immerse immediately in silver nitrate solution (1 in 50) for 1 minute, and rinse again in purified water. Expose the cut surface of bone, in water, to daylight or another source of actinic light until the calcified areas develop a clearly defined stain without marked discoloration of the uncalcified areas. The staining procedure may be modified to differentiate more clearly between calcified and uncalcified areas.

Score the degree of calcification of the rachitic metaphysis in each rat, according to a scale which allows the average response to be plotted as a straight line against the logarithm of the dose. The figure presented illustrates the range of the degree of calcification best suited for assay purposes.

Acceptability—Observations are acceptable for use in calculation of the potency only from those groups in which two-thirds or more but not less than 7 rats show calcification at least as great as the lowest level and not greater than the highest level illustrated in the figure. If the average score of the standard group on the high dosage level is not greater than the average score of the standard group on the low dosage level, discard the results and repeat the assay. If an assay sample is represented solely by assay groups which are not acceptable for measuring vitamin D potency and in each of which the average score is less than the average score of the standard group on the low dosage level or more than the average score of the standard group on the high dosage level, its assayed content of vitamin D is respectively less than that represented by the low dose or more than that represented by the high dose of the Reference Standard.

Calculation—Tabulate the scores (y), listing each litter in a separate row with treatment groups in columns. Omit any groups which do not meet the test for *Acceptability*. Equalize the number of observations in the acceptable groups by disregarding the results on all litters not equally represented in the groups or by other suitable means (see *Design and Analysis of Biological Assays*, USP XVIII). Total the f scores for each of the treatment groups, where f is the number of litters, and designate each total as T with subscripts 1 and 2 for the low and high dosage levels, respectively. Compute the slope b from the sums of T_1, *i.e.*, ΣT_1, and of T_2, *i.e.*, ΣT_2, for the standard and sample, provided the latter is represented at both dosage levels as $b = (\Sigma T_2 - \Sigma T_1)/ifk'$, where i is the logarithm of the ratio of the high dose to the low dose and is the same for each preparation, and k' is the number of preparations represented by two dosage levels and included in the calculation of the value of b.

Compute the logarithm of the relative potency of each sample under assay as log (relative potency) $= M' = (\bar{y}_T - \bar{y}_S)/b = ik'T_s - 2\Sigma T_s$, where each mean score, $\bar{y}_T$ for the assay sample and $\bar{y}_S$ for the Reference

Standard, is the average of the individual scores for an intermediate dosage level or of the two means for the high and the low dosage levels and where $T_3 = \Sigma T_2 - \Sigma T_1$ and T_4 is defined in USP XVIII. Convert each observed M' to its antilogarithm to obtain the relative potency of the sample. Multiply the relative potency by the assumed potency of the assay oil in Units per g., adopted at the start of the assay, to obtain its assayed content of vitamin D in USP Units per g.

Chemical Method

The following procedure is provided for the determination of vitamin D as an ingredient of official preparations containing other active constituents.

Special Reagents and Solutions—

Chromatographic Fuller's Earth—Use chromatographic fuller's earth having a water content corresponding to not less than 8.5 percent and not more than 9.0 percent of loss on drying.

Solvent Hexane—Use reagent solvent hexane (see USP XVIII), distilling if necessary so that it meets the following additional specification:

Spectral purity—Measure in a 1-cm. cell at 300 mμ, with a suitable spectrophotometer, against air as the blank: the absorbance is not more than 0.070.

Ethylene Dichloride—Purify by passage through a column of granular (20 to 200 mesh) silica gel.

Potassium Hydroxide Solution—Dissolve 780 g. of potassium hydroxide in water to make 1000 ml.

Cottonseed Oil—Use cottonseed oil USP that meets the following additional requirement: Saponify 10 g. of the oil as directed in this chapter under *Sample Preparation*, beginning with "then add a volume of *Potassium Hydroxide Solution*," and dissolve the unsaponifiable residue in 10 ml. of *Solvent Hexane*.

In a separate container place 0.4 ml. of ferric chloride solution (1 in 1000) and 12 ml. of a 1 in 6000 solution of 2,2'-bipyridine in dehydrated alcohol, mix, and 5 minutes later read the absorbance in a 1-cm. cell at 520 mμ, with a suitable spectrophotometer, using dehydrated alcohol as the blank. Then add 0.2 ml. of the solvent hexane solution of the unsaponifiable residue, and after 5 minutes read the absorbance. The difference between the first and the second absorbances is not less than 0.125.

Color Reagent—Prepare two stock solutions as follows.

Solution A—Empty, without weighing, the entire contents of a previously unopened 113-g. bottle of dry, crystalline antimony trichloride into a flask containing about 400 ml. of *Ethylene Dichloride*. Add about 2 g. of anhydrous alumina, mix, and filter through filter paper into a clear-glass, glass-stoppered, container calibrated at 500 ml. Add *Ethylene Dichloride* to make 500 ml., and mix: the absorbance of the solution, measured in a 2-cm. cell at 500 mμ, with a suitable spectrophotometer, against *Ethylene Dichloride*, does not exceed 0.070.

Solution B—Mix, under a hood, 100 ml. of acetyl chloride and 400 ml. of *Ethylene Dichloride*.

Mix 45 ml. of *Solution A* and 5 ml. of *Solution B* to obtain the *Color Reagent*. Store in a tight container, and use within 7 days, but discard any reagent in which a color develops.

Chromatographic Tubes—

First Column—Arrange for descending column chromatography (see page 786) a tube of 2.5 cm. (inside) diameter, about 25 cm. long, and constricted to 8 mm. diameter for a distance of 5 cm. at the lower end, by inserting at the point of constriction a coarse-porosity, sintered-glass disk or a small plug of glass wool. The constricted portion may be fitted with an inert, plastic stopcock.

Second Column—Select a tube that is made up of three sections: (1) a flared top section, 18 mm. in (inside) diameter and approximately 14 cm. long, (2) a middle section, 6 mm. in (inside) diameter and approximately 25 cm. long, and (3) a tapered, constricted lower exit tube approximately 5 cm. long. Insert a small plug of glass wool in the upper 1-cm. portion of the constricted section.

Chromatographic Columns—

First Column—To about 125 ml. of isooctane contained in a screw-cap, wide-mouth bottle add 25 g. of chromatographic siliceous earth, and shake until a slurry is formed. Add, dropwise and with vigorous mixing, 10 ml. of polyethylene glycol 600. Replace the bottle cover, and shake vigorously for 2 minutes. Pour about half of the resulting slurry into the chromatographic tube, and allow it to settle by gravity. Then apply gentle suction, and add the remainder of the slurry in small portions, packing each portion with a 20-mm. disk plunger. When a solid surface has formed, remove the vacuum, and add about 2 ml. of isooctane.

Second Column—Pack the midsection of the tube with 3 g. of moderately coarse *Chromatographic Fuller's Earth* with the aid of gentle suction (about −125 mm. of mercury).

Standard Preparation—Dissolve about 25 mg. of USP Ergocalciferol Reference Standard, accurately weighed, in sufficient isooctane to make 100.0 ml. Store in a refrigerator.

On the day of assay, pipet 1.0 ml. of the standard solution into a 50-ml. volumetric flask, remove the solvent with a stream of nitrogen, and dissolve the residue in, and dilute to volume with, *Ethylene Dichloride*.

Sample Preparation—Unless otherwise

directed, accurately weigh or measure a portion of the sample to be assayed, equivalent to not less than 125 mcg. but preferably about 250 mcg. of ergocalciferol (10,000 USP Units). If little or no vitamin A is present in the sample, add about 1.5 mg. (the equivalent of 5000 USP Units) of vitamin A to provide the needed pilot bands in the subsequent chromatography.

For capsules or tablets, reflux not less than 10 of them in 10 ml. of water on a steam bath for about 10 minutes, crush the remaining solid with a blunt glass rod, and warm for 5 minutes longer.

Add 2 ml. of *Cottonseed Oil*, then add a volume of *Potassium Hydroxide Solution* representing 2.5 ml. for each g. of the total weight of the sample plus cottonseed oil, but not less than 15 ml. Add 50 ml. of alcohol. Reflux vigorously on a steam bath for 20 minutes, or for 30 minutes for samples weighing more than 5 g. If oil globules are evident, indicating incomplete saponification, add 5 ml. of *Potassium Hydroxide Solution* (but not exceeding a total of 100 ml.), and heat again. Cool, and transfer the saponified mixture to a 500-ml. separator, rinsing the saponification flask with a total of 50 ml. of water and adding each rinse to the separator. Add about 4.5 g. of sodium sulfate decahydrate and 150 ml. of *Solvent Hexane*. Shake vigorously for 2 minutes. When the aqueous layer has separated, transfer it to a second separator. Extract with two 50-ml. portions of *Solvent Hexane*, combine the extracts, and discard the aqueous solution.

Wash the combined solvent hexane extracts with 50-ml. portions of water until the last portion shows no pink color on the addition of phenolphthalein T.S. Allow the washed extract to stand for 5 minutes, discard any water that separates, and transfer the extract to a 300-ml. tall form beaker containing about 5 g. of anhydrous sodium sulfate. Stir for 2 minutes, and decant the solution into a 500-ml., tall-form beaker. Rinse the sodium sulfate with four 25-ml. portions of *Solvent Hexane*, combining the rinsings with the original extract. Reduce the total volume to about 30 ml. by evaporation on a steam bath, and transfer the concentrate to a small, round-bottom evaporation flask. Rinse the beaker with four 5-ml. portions of *Solvent Hexane*, adding the rinsings to the flask. With the aid of vacuum in a water bath at a temperature not exceeding 40°, or with a stream of nitrogen at room temperature, remove the remaining solvent completely. Dissolve the residue in a small amount of *Solvent Hexane*, transfer to a 10-ml. volumetric flask, and dilute with *Solvent Hexane* to volume to obtain the *Sample Preparation*

Procedure—

First Column Chromatography—Just as the 2 ml. of isooctane disappears into the surface of the prepared *First Column*, pipet 2.0 ml. of the *Sample Preparation* onto the column. As the meniscus of the *Sample Preparation* reaches the column surface, add the first of three 2-ml. portions of *Solvent Hexane*, adding each succeeding portion as the preceding portion disappears into the column. Continue adding *Solvent Hexane* in portions of 5 to 10 ml. until 100 ml. has been added. If necessary, adjust the flow rate to between 3 and 6 ml. per minute, by application of gentle pressure at the top of the chromatographic tube.

Discard the first 20 ml. of effluent, and collect the remainder. Examine the column under ultraviolet light at intervals during the chromatography, and stop the flow when the front of the fluorescent band representing vitamin A is about 5 mm. from the bottom of the column. (The ultraviolet lamp should provide *weak* radiation in the 300-mμ region. It is frequently necessary to use a narrow aperture or screen with commercial lamps to reduce the amount of radiation to the minimum required to visualize the vitamin A on the column.)

Transfer the eluate to a suitable evaporation flask, and remove the solvent hexane completely under vacuum at a temperature not above 40°, or with a stream of nitrogen at room temperature. Dissolve the residue in about 10 ml. of *Solvent Hexane*.

Second Column Chromatography—Add the solvent hexane solution obtained as directed under *First Column Chromatography* onto the *Second Column*. Rinse the evaporation flask with a total of 10 ml of solvent hexane in small portions, adding each portion to the *Second Column* and allowing it to flow through the column, and discard the effluent. When about 1 ml. of the solvent hexane remains above the surface of the column, add 75 ml. of benzene, and elute with the aid of gentle suction (about 125 mm. of mercury), collecting the eluate. Evaporate the benzene under vacuum at a temperature not above 40°, or with a stream of nitrogen at room temperature.

Assay Preparation—Dissolve the residue obtained as directed under *Second Column Chromatography* in a small amount of *Ethylene Dichloride*, transfer to a 10-ml. volumetric flask, and dilute to volume with *Ethylene Dichloride* to obtain the *Assay Preparation*.

Color Development—Into each of three suitable, matched colorimeter tubes of about 2-cm. diameter, and designated *1*, *2*, and *3*, respectively, pipet 1.0 ml. of the *Assay Preparation*. Into tube *1* pipet 1.0 ml. of the *Standard Preparation*, into tube *2*, 1.0 ml. of *Ethylene Dichloride*, and into tube *3*, 1.0 ml. of a mixture of equal volumes of acetic anhydride and *Ethylene Dichloride*. To each tube add quickly, and preferably from an automatic pipet, 5.0

ml. of *Color Reagent*, and mix. Exactly 45 seconds after the addition of the color reagent, determine the absorbances of the three solutions at 500 mμ, with a suitable spectrophotometer, using *Ethylene Dichloride* as the blank. Similarly, 15 seconds after making the first reading on each solution, determine the absorbances of the solutions in tubes 2 and 3 at 550 mμ, in a similar manner. Designate the absorbances as A^1_{500}, A^2_{500}, A^3_{500}, A^2_{550}, and A^3_{550}, respectively, in which the superscript indicates the number of the tube and the subscript the wavelength.

Calculation—Calculate the quantity, in meg., of vitamin D in the portion of the sample taken by the formula $(C_S/C) \times (A_U/A_S)$, in which C_S is the concentration of vitamin D in meg. per ml. of the *Standard Preparation*, C is the concentration of the sample (as g., capsules, tablets, etc.) in each ml. of the final solution, A_U has the value of $(A^2_{500} - A^3_{500}) - 0.67(A^2_{550} - A^3_{550})$ determined from the absorbances observed on the solution from the *Assay Preparation*, and A_S has the value of $A^1_{500} - A^2_{500}$ determined on the solution from the *Standard Preparation*.

VOLUMETRIC APPARATUS

Most of the volumetric apparatus available in the United States is calibrated at 20°, although the temperatures generally prevailing in laboratories more nearly approach 25°, which is the temperature specified generally for National Formulary tests and assays. This discrepancy is inconsequential provided the room temperature is reasonably constant and the apparatus has been calibrated accurately prior to and under the conditions of its intended use.

Use—To attain the degree of precision required in many NF assays involving volumetric measurements and directing that a quantity be "accurately measured," the apparatus must be chosen and used with exceptional care. Where less than 10 ml. of titrant is to be measured, a 10-ml. buret or microburet generally is required.

The design of volumetric apparatus is an important factor in assuring accuracy. For example, the length of the graduated portions of graduated cylinders should be not less than five times the inside diameter, and the tips of burets should permit an outflow rate of not more than 0.5 ml. per second.

Standards of Accuracy—The capacity tolerances for volumetric flasks, transfer pipets, and burets are those accepted by the National Bureau of Standards,* as indicated in the accompanying tables.

The capacity tolerances for measuring (*i.e.*, "graduated") pipets of up to and including 10-ml. capacity are somewhat larger than those for the corresponding sizes of transfer pipets, namely, 10, 20, and 30 μl. for the 2, 5, and 10-ml. sizes, respectively.

Transfer and measuring pipets calibrated "to deliver" should be drained in a vertical position and then touched against the wall of the receiving vessel to drain the tips. Volume readings on burets should be estimated to the nearest 10 μl. for 25 and 50-ml. burets, and to the nearest 5 μl. for 5 and 10-ml. burets. Pipets calibrated "to contain" are called for in special cases, generally for measuring viscous fluids like syrups. In such cases, the pipet should be washed clean, after draining, and the washing added to the measured portion.

* See "Testing of Glass Volumetric Apparatus," NBS Circ. 602, April 1, 1959.

Volumetric Flasks

Designated volume, ml.	10	25	50	100	250	500	1000
Limit of error, ml.	0.02	0.03	0.05	0.08	0.12	0.15	0.30
Limit of error, percent	0.20	0.12	0.10	0.08	0.05	0.03	0.03

Transfer Pipets

Designated volume, ml.	1	2	5	10	25	50	100
Limit of error, ml.	0.006	0.006	0.01	0.02	0.03	0.05	0.08
Limit of error, percent	0.60	0.30	0.20	0.20	0.12	0.10	0.08

Burets

Designated volume, ml.	10 ("micro" type)	25	50
Subdivisions, ml.	0.02	0.10	0.10
Limit of error, ml.	0.02	0.03	0.05

EXCERPT FROM PLAINTIFFS' SUPPLEMENTAL MEMORANDUM RESPONDING TO QUESTION OF DISTRICT COURT

IV.

A. Plaintiff Solgar Co., Inc.: The $50,000 cost for relabeling and reformulation constitutes approximately 14 percent of the company's operating expenses and approximately one-third of its net profits.

B. Leeds-Dixon Laboratories, Inc.: The $75,000 expenditure on the part of said company constitutes approximately 8 percent of its operating expenses.

C. Solgar Co., Inc. sells the following dosage forms of vitamins A and D:

Vitamin A - 5,000 IU, 10,000 IU, 25,000 IU.
Vitamin D - 400 IU, 1,000 IU, 2,000 IU, 2,500 IU.

D. Leeds-Dixon Laboratories, Inc. sells the following dosage forms of vitamins A and D:

Vitamin A - 5,000 IU, 10,000 IU, 12,500 IU, 15,000 IU, 25,000 IU.

Vitamin D - 400 IU. Lower dosages are found naturally in various foods.

NLR:vk

AFFIDAVIT OF NAOMI L. REICE
(Filed September 20, 1973)

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

THE NATIONAL NUTRITIONAL FOODS ASSOCIATION and SOLGAR CO, INC.,

Plaintiffs,

-against-

CASPAR W. WEINBERGER, Secretary of Health, Education and Welfare, and ALEXANDER M. SCHMIDT, Commissioner of Food and Drugs,

Defendants.

AFFIDAVIT

73 Civ. 3448 (MEF)

STATE OF NEW YORK)
COUNTY OF NEW YORK : ss.:
SOUTHERN DISTRICT OF NEW YORK)

NAOMI L. REICE, being duly sworn, deposes and says:

1. I am an Assistant United States Attorney in the office of Paul J. Curran, the United States Attorney for the Southern District of New York, attorney for defendants. I submit this affidavit to set forth for the Court certain information which has been furnished to this office by the Public Health Service of the Food and Drug Administration. The letters accompanying the transmission of the information are annexed hereto as Exhibits A and B.

2. The information contained in this affidavit relates to certain statements contained in Part IV. of plaintiffs' Supplemental Memorandum about the operations of plaintiff Solgar Co., Inc. ("Solgar") and Leeds-Dixon Laboratories, Inc., ("Leeds-Dixon") which markets its products under the "Schiff" Label.

3. In Point IV of plaintiffs' memorandum it is stated that Solgar sells Vitamin A is the following dosage units: 5,000 IU, 10,000 IU and 25,000 IU. Annexed hereto as Exhibit C is a label of Solgar which reflects a 50,000 unit

NLR:vk

vitamin A capsule among its product line.

4. Annexed hereto as Exhibit D is Solgar's label for a product called "Super-Plex" for which Solgar suggests a dosage of 3 to 6 tablets daily. If six tablets are consumed, 30,000 units of Vitamin A are ingested.

5. As to Leed-Dixon, plaintiffs informed the Court that it sells Vitamin D in units of 400 IU. On page 13 of Leeds-Dixon's (Schiff's) catalogue is listing for "Halibut Liver Oil Capsules" represented as containing 850 units of Vitamin D. See Exhibit E.

6. Moreover, if a consumer takes Leeds-Dixon's "Gerimost" tablets as directed, See Exhibit F, page 10 of catalogue, a consumer would ingest 1,000 units of vitamin D.

7. It is recognized that the information contained in this affidavit is not absolutely current, but it is the latest information on file with the FDA and, if still accurate, highly relevant.

S/

NAOMI L. REICE
Assistant United States Attorney

Sworn to before me
this 19th day of September

[illegible]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

ABLE ADDRESS: NYFOODRUG

NEW YORK DISTRICT
850 THIRD AVENUE
BROOKLYN, NEW YORK 11232
TELEPHONE: (212) 788-5000

Honorable Paul J. Curran
United States Attorney
Southern District of New York
United States Court House
Foley Square
New York, New York 10007

Attention: Naomi L. Reice
Ass't U.S. Attorney

Re: Solgar Co., Inc.
New York, New York

Dear Madam:

Pursuant to a request from Mr. Steve McNamara of the General Counsel's office of the U.S. Food and Drug Administration on 9/14/73, please be advised that the New York District office of the U.S. Food and Drug Administration conducted an inspection at the above referenced firm which was completed on August 8, 1971. It was determined at that time that Solgar Company was a manufacturer, repacker and relabeler of a long line of vitamin products marketed under their name.

Enclosed are examples of labels of vitamin A and vitamin D containing products that were collected during that inspection.

We would appreciate you returning the labels to this office when you have finished with them.

Yours truly,

TED M. HOPES
Acting Director
Compliance Branch
New York District

/jpb

EXHIBIT A

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

September 14, 1973

NEWARK DISTRICT
ROOM 831 - 970 BROAD STREET
NEWARK, NEW JERSEY 07102
TELEPHONE: 201-645-2844

Honorable Paul J. Curran
U.S. Attorney for the Southern
District of New York
U.S. Court House, Foley Square
New York, N.Y. 10007
c/o A.U.S.A. Naomi L. Reice

Dear Sir,

RE: Leeds-Dixon Laboratories Corp.
Moonachie, New Jersey

Pursuant to a request from Mr. Steve McNamara of the General Counsel's office of the U.S. Food and Drug Administration on 9/14/73, please be advised that the Newark District office of the U.S. Food & Drug Administration conducted an inspection at the above referenced firm which was completed on 6/23/72. It was determined at that time that Leeds-Dixon Laboratories manufactures a long line of vitamin preparations and packages them under the "Schiff Bio-foods product Inc." label. These vitamin preparations are the firm's main line of dietary supplements.

Enclosed is a catalogue of Schiff products obtained during the inspection at Leeds-Dixon Laboratories, Moonachie, N.J., which shows that most of the products are offered under the "Schiff" label.

We would appreciate your returning the catalogue to this office upon completion of your use.

George Troublefield
Acting Director Compliance Branch
Newark District

GT/dj

Enclosure

EXHIBIT B

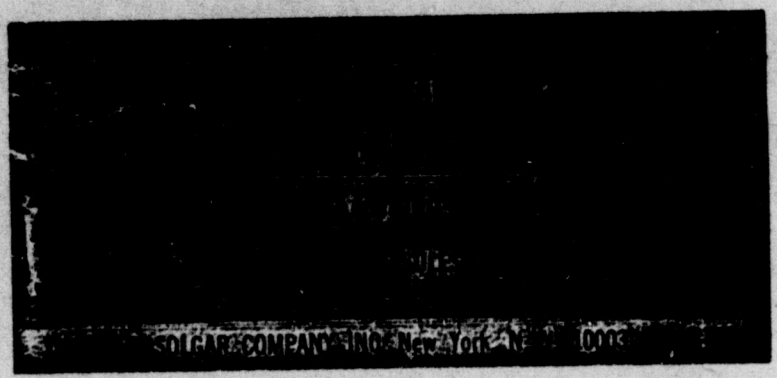


EXHIBIT C

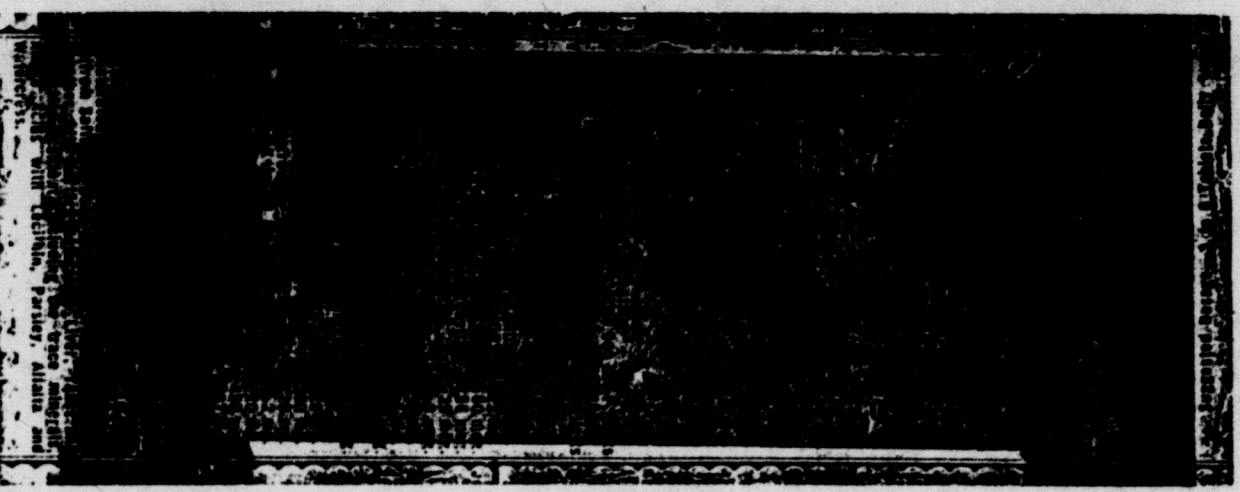


EXHIBIT D

ALL-NATURAL VITAMIN CATALOG AND DIGEST

VOL. 12 NO. 1

QUALITY Schiff NATURAL

EMULSIFIED A CAPS/HALIBUT LIVER OIL CAPS
VITAMIN A CAPS/A-D DROPS

VITAMIN A

Emulsified A Capsules

For Greater Digestibility

Livers from the freshest fish available, a pectin emulsifier to reduce the size of the fat globules—and you get the perfect, most digestible Vitamin A supplement. 25,000 unit capsules.

EMULSIFIED A Capsules		
100	250	500
$1.95	$4.35	$7.95

Halibut Liver Oil Capsules

Natural Vitamin A in Tiny 3 Minim Capsules!

"Gourmet" health preferences? Get your Vitamin A as well as 850 units of Vitamin D from the livers of fresh halibut. 5,000 units Vitamin A and 850 units Vitamin D.

HALIBUT LIVER OIL Capsules	
100	250
$1.00	$2.25

Vitamin A Capsules

Many Oils in One Capsule

Our "perles" of health, derived from a potpourri of the finest deep-sea fish, and swallowed with the greatest of ease. 25,000 unit caps.

VITAMIN A Capsules		
100	250	1,000
$1.65	$3.75	$14.00

A-D Drops

5,000 Units of A in Only 3 Drops

Add 500 units of Vitamin D and you have 125% of the MDR for both Vitamins A and D. All this in only 3 drops daily and no need to swallow capsules. One bottle contains 450 drops distilled from the finest fish liver oils.

A-D DROPS
1 oz.
$2.50
(5 months' supply)

GERIMOST For the Mature
NUCLE-BEC

Gerimost

Schiff Has Designed A High Potency Vitamin-Mineral-Enzyme Formula Specifically for the Mature in Easy to Take Dosage Form

The step slows a little, interest in daily living may lag, preparing food and eating become a chore, some foods are not tolerated as well as before. This is the story of too many people who face maturity.

And so the dietary intake suffers, the step becomes even slower, and interest in daily activity wanes. But many mature people have discovered that this need not be. They have learned how to break the negative cycle, by following Schiff's healthful regimen: ample sleep, avoiding stress, exercise and sensible nutrition. For only when the diet is complete with essential nutrients, can the negative cycle be broken.

GERIMOST, the quality formula for the mature, that offers all these features:

■ Two piece capsule; ■ More Vitamin E from unesterified tocopherols; ■ More iron; ■ More pancreatic enzymes; ■ More soluble bioflavonoids; ■ Instant dissolvability for greater absorbability; ■ Easily swallowed; ■ May be easily opened to mix into food.

GERIMOST Capsules		
90	180*	360
$4.25	$7.90	$14.50

*month's supply

GERIMOST ANALYSIS
2 capsules with each meal (6 daily)

NATURAL VITAMINS	
Vitamin A	25,000 USP Units
Vitamin D	1,000 USP Units
Vitamin B-1	7 mg.
Vitamin B-2	14 mg.
Vitamin C	200 mg.
Niacin	4.50 mg.
Cobalamin (B-12 Activity)	25 mcg.
Vitamin E (d-alpha)	10 int. Units
Bioflavonoids (water soluble) plus Hesperidin, Rutin	40 mg.
NATURAL MINERALS	
Calcium	550 mg.
Phosphorus	200 mg.
Iron	40 mg.
Iodine	0.1 mg.
Magnesium	40 mg.
ENZYMES	
Natural Enzymes From Pancreas	
Protease, Diastatic, Lipolytic	100 mg.
Pepsin	50 mg.
Plus many other natural food factors:	
Glutamic Acid	75 mg.
Nucleic Acid	75 mg.

Nucle-BEC

Nucleic Acid Fortified with Three Important Vitamins B, E and C.

You have probably read about the interesting research which is being conducted on Nucleic Acid. Now Schiff brings you Nucle-BEC, a substantial Nucleic Acid formula.

In addition to 100 mg. of Nucleic Acid, Schiff Nucle-BEC is fortified with large amounts of 6 more nutrients — all essential to your system. You get 4 of the most important B Vitamins; plus over 3 times the MDR of Rose Hips C, plus 50 I.U. of Vitamin E. All natural.

NUCLE-BEC Tablets		
60	120	240
$3.25	$5.75	$9.50

EXHIBIT F

OPINION OF DISTRICT COURT DENYING PLAINTIFFS' MOTION FOR A PRELIMINARY INJUNCTION

(Filed September 25, 1973)

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

THE NATIONAL NUTRITIONAL FOODS ASSOCIATION and SOLGAR CO., INC.,	
Plaintiffs,	
-against-	
CASPAR W. WEINBERGER, Secretary of Health, Education and Welfare, and ALEXANDER M. SCHMIDT, Commissioner of Food and Drugs,	MEMORANDUM
Defendants.	73 Civ. 3448

FRANKEL, D.J.

On October 1, 1973, regulations of the Food and Drug Administration will become effective requiring that preparations of Vitamin A and Vitamin D in excess of 10,000 I.U. (international units) per dosage unit and 400 I.U. per dosage unit, respectively, shall be restricted to prescription sale and that such vitamins shall be labelled accordingly. The regulations read as follows:

21 C.F.R. §3.94

"(a) Vitamin A is an essential nutrient for humans. It is widely recognized that large amounts of vitamin A can cause adverse effects, some of which are serious. The U.S. Recommended Daily Allowance (U.S. RDA) for vitamin A is 1500 International Units, (IU) for infants, 2500 IU for children under 4 years of age, 5000 IU for adults and children 4 or more years of age, and 8000 IU for pregnant or lactating women.

"(b) In view of the toxicity of excessive consumption of vitamin A, the Food and Drug Administration finds that, in order to protect the public health, oral preparations containing vitamin A in excess of 10,000 IU per dosage unit or recommended daily intake are drugs subject to section 503 (b)(1) of the Federal Food, Drug, and Cosmetic Act and shall be restricted to prescription sale. Such products will be regarded as misbranded if at any time prior to dispensing the following conditions are not met:

"(1) The label bears the legend. 'Caution: Federal law prohibits dispensing without a prescription'; and

"(2) The labeling bears full disclosure information as required by §1.106(b)(3)(i) of this chapter, and especially appropriate warnings regarding vitamin A toxicity.

"(c) Preparations containing 10,000 or less IU of vitamin A per dosage unit will be regarded as misbranded if their recommended daily intake exceeds 10,000 IU."

'21 C.F.R. §3.95

"(a) Vitamin D is an essential nutrient for humans. It is widely recognized that vitamin D, when ingested daily in large amounts, is toxic. The U.S. Recommended Daily Allowance (U.S. RDA) for vitamin D is 400 International Units (IU).

"(b) In view of the toxicity of the excessive consumption of vitamin D, the Food and Drug Administration finds that, in order to protect the public health, oral preparations containing vitamin D in excess of 400 IU per dosage unit or recommended daily intake are drugs subject to section 503(b)(1) of the Federal Food, Drug, and Cosmetic Act and shall be restricted to prescription sale. Such products will be regarded as misbranded if at any time prior to dispensing the following conditions are not met:

"(1) The label bears the legend, 'Caution: Federal law prohibits dispensing without a prescription'; and

"(2) The labeling bears full disclosure information as required by §1.106(b)(3)(i) of this chapter, and especially appropriate warnings regarding vitamin D toxicity.

"(c) Preparations containing 400 or less IU of vitamin D per dosage unit will be regarded as misbranded if their recommended daily intake exceeds 400 IU.

"(d) Foods which are represented for use solely under medical supervision to meet nutritional requirements of persons with poor vitamin D absorption may contain vitamin D not in excess of 1000 IU per dosage unit or recommended daily intake."

[redacted]

This is an action charging that the quoted regulations are invalid and seeking to enjoin their enforcement. The plaintiffs have moved for a preliminary injunction. The extraordinary relief thus sought must be denied upon the findings of fact and conclusions of law outlined below.

The plaintiffs are the National Nutritional Foods Association, a trade association composed of manufacturers, wholesalers, and retailers of vitamins and dietary supplements, and Solgar Co., Inc., a New York corporation which manufactures, distributes, and sells vitamin supplements.

The immediate background of the regulations in question begins with their promulgation by the Commissioner of Food and Drugs as proposed regulations in the Federal Register dated December 19, 1972 (37 Fed. Reg. 26618). These regulations were corrected in minor detail in the Federal Register dated January 4, 1973 (38 Fed. Reg. 799). The Commissioner promulgated these regulations for the "efficient enforcement"

of §§502(a), (f), and (j), and 503(b) of the Food and Drug Act as authorized by 21 U.S.C. §371(a), under powers delegated to him by the Secretary. 21 C.F.R. §2.120.

Explaining what were then his tentative views, the Commissioner said:

> "The acute and chronic toxicity of these vitamins is documented extensively in the medical literature. Vitamin A is available over the counter in dosage levels up to 10 times the recommended daily dietary allowance (RDA) of the Food and Nutrition Board, National Academy of Sciences-National Research Council (NAS-NRC) and vitamin D is available up to 60 times the RDA. The availability without prescription of these vitamins in high dosage levels contributes significantly to their misuse and the occurrence of serious adverse effects." (37 Fed. Reg. 26618 (1972)).

Adverse effects which the Commissioner found from excessive intake of Vitamin A include among others anorexia, growth retardation in children, migratory arthralgia and intracranial pressure. Adverse effects resulting from an excess of Vitamin D include anorexia, weight loss, polyuria, certain forms of calcification, hypertension, anemia, irreversible renal failure and death. In respect of

Vitamin D the Commissioner noted that some of these severe effects are irreversible, and that the margin of safety between nutritional requirements and toxic levels is small.

An extensive bibliography listing the scientific articles used by the FDA in formulating its proposed regulation was placed on public view.

When the Commissioner published the proposed rules and their rationale he provided 60 days in which interested parties might comment, in accordance with the rulemaking provisions of the Administrative Procedure Act. (5 U.S.C. §553(c)). The response was massive. Over 2500 comments were received. Of special interest for present purposes, the two plaintiffs herein, as well as other drug companies, presented substantial amounts of factual material and expert opinion opposing the proposed regulations. Others made extensive submissions pro and con. The mass of these presentations has been lodged with the court and fills some 45 manila folders.

The commentators, responding to the Commissioner's invitation, fell into three general categories:

(1) Those who agreed that prescription levels are necessary and that those proposed by the FDA were suitable. This group included official representatives of the American Academy of Pediatrics, the American Medical Association, the American Dietetic Association, and other medical and scientific experts.[1]

(2) Those who agreed that prescription levels were necessary but argued that the levels should be higher than those set by the FDA. These groups included most drug manufacturers and trade associations as well as a few individual consumers.

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1. One group of commentators, mainly scientists and medical researchers, argued that the Commissioner should actually set lower unit limits for prescription sales.

Several of these commentators made a critical review of the scientific literature used by the FDA, arguing generally that "toxicity below 50,000 I.U. daily for vitamin A was rare and that vitamin D toxicity reports would not support the vitamin D level proposed." (38 Fed. Reg. 20724 (1973)).

(3) Those who disagreed with the proposal entirely, arguing that vitamins are foods and that individuals should have the right to use any amounts they desire. Most individual consumer comments as well as comments from health food retailers fell in this category. Such commentators pointed out that the dosage level of vitamins in many foods is higher than the prescription level - for example, 100 grams of liver contains at least 24,000 I.U. of vitamin A - and that a limitation on vitamins and not on food substances is irrational.

Having considered the factual and legal materials submitted for his expert judgment, the Commissioner concluded that the regulations now assailed should be adopted. (38 Fed. Reg. 20723 (1973)).

As grounds for this determination he noted that:

> "The concern of the Food and Drug Administration is the availability of vitamin A and vitamin D in large dosage units in medicinal forms, i.e., capsules and tablets, particularly in view of the multiplicity of other sources of this vitamin in the daily diet. The convenience of ingestion in this form on a routine basis encourages excessive intake of these vitamins far beyond the average amounts ingested in normal diets of conventional food over extended periods of time. Adequate amounts of vitamin A and vitamin D will continue to be available as dietary supplements and are not being removed from the market place. The margins of safety provided in the levels established by this proposal were developed to take into account the wide ranges of vitamin content in foods and the dosage levels of vitamin A and vitamin D preparations that are usually implicated in toxic conditions." (38 Fed. Reg. 20724 (1973)).

Aiming to establish a reasonable "margin of safety," the Commissioner concluded that the limits he had proposed were prudent and efficacious.

In support of their claim that the Commissioner's regulations are not valid - and, more immediately, that the invalidity and resulting injury are clear enough to warrant the extraordinary relief of a preliminary injunction - the plaintiffs argue that:

(1) The Commissioner has exceeded his statutory authority in that he has improperly classified vitamins as drugs when they are in fact food substances and beyond the range of the Commissioner's authority to regulate.

(2) In any case vitamins, even if classified as drugs, cannot be defined as a "prescription drug" within the ambit of 21 U.S.C. §353, which these regulations are designed to effectuate.

(3) The Commissioner's decision to require prescription limitations for vitamin A and D is not supported by the medical and scientific evidence and is factually unreasonable.

None of these claims can be sustained.

(1) Plaintiffs argue that vitamins are food substances and thus not subject to FDA regulations as "drugs." The Commissioner has made the judgment, however, that vitamins are a food only when used within the limits of the recommended daily allowance. At such a level they, like ordinary foods, are "nutrients." Above those levels they are deemed "appropriate only for therapeutic purposes and thus are properly classified as drugs" (38 Fed. Reg.

20723 (1973)).

21 U.S.C. §321(g)(1) defines the term "drug" as follows:

> "(A) articles recognized in the official United States Pharmacopeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any article specified in clauses (A), (B), or (C) of this paragraph; but does not include devices or their components, parts, or accessories."

This language is to be construed liberally in the light of the statutory concern for health and safety. See, e.g., United States v. Bacto-Unidisk, 394 U.S. 784, 792 (1969); United States v. Sullivan, 332 U.S. 689, 693-97 (1948); United States v. Dotterweich, 320 U.S. 277, 280 (1943); United States v. Diapulse Corporation of America, 457 F.2d 25, 28 (2d Cir. 1972). Quite apart from rules of construction, and leaving aside the lay knowledge that the likeliest place to go for vitamins is the "drug store," the

products here are squarely within the literal language and evident meaning of the statute. If there were more doubt, the question would surely be one on which to weigh further against plaintiffs the everyday experience and judgmental responsibility of the Commissioner. N.L.R.B. v. Hearst Publications, 322 U.S. 111, 130 (1944).

(2) Plaintiffs argue that even if Vitamins A and D are to be denominated "drugs," they do not fall within the statutory definition of a "prescription drug" subject to the kind of regulatory authority the Commissioner has asserted. The provision in question is 21 U.S.C. §353, which states in relevant part:

> "(b)(1) A drug intended for use by man which—
>
> * * *
>
> "(E) because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, is not safe for use except under the supervision of a practitioner licensed by law to administer such drug
>
> * * *
>
> shall be dispensed * * * upon * * * prescription * * *."

It is plain that the concern over "potentiality for harmful effect" imposes broad responsibility upon the Commissioner to safeguard human health. He has acted well within that duty in setting upper limits at a level convenient and agreeable for affected consumers (including those who may want two or three pills to reach levels recommended by the most exuberant of vitamin enthusiasts) while affording protection through a safety margin against dangers which have been universally acknowledged even if they are not mechanically quantifiable at a precisely agreed level. The Commissioner is not only entitled but required to be at least as prudent as lay understanding of human behavior would dictate. He knows that almost nobody has a reliably identified need for as much as - let alone more than - 10,000 daily units of Vitamin A.[2]

2. Comparable observations apply to Vitamin D.

He knows, because we all do, of the prevalent wisdom among us pill swillers that "if one is good, two are better." He knows such things as the widely held belief in the efficacy of Vitamin A for acne, and he knows that moderation may not be the chief attibute of those troubled by this condition. Knowing such obvious things and other matters less patent, the Commissioner is not required to circumscribe his reponsibilities in terms solely of the completely "rational" consumer. He may and he must consider the "potentiality for harmful effect" through excessive use to the merely "average" man and even to the substantial numbers of us who help create the average by falling below it.

Both plaintiffs and defendants agree that toxicity exists at some level. Plaintiffs' quarrel with the Commissioner is over the dosage point at which some restrictions would become prudent. The Commissioner, however, is not required to set the over-the-counter limit at a maximum which the consumer (be he old, young, weak or strong) might withstand. See United States v. Rodine Products, 206 F. Supp. 201, 207 (D.Ariz. 1962).

A substantial margin of safety probably should - certainly may - be used, at least in a case like this, where it can have only beneficial effects for the Commissioner's paramount subject of health.

> "One making a rule for the future which in practical effect will determine whether millions of people shall eat something everyday may reasonably refuse to subject the general public to even slight risks and small deceptions." Atlas Powder v. Ewing, 201 F.2d 347, 355 (3d Cir. 1952).

(3) Plaintiffs launch a variety of procedural and "evidentiary" attacks upon the factual premises of the regulations. None of these seems meritorious.

The Commissioner's judgments about safety levels (in the admittedly uncertain and debated state of knowledge) and consumer habits are solidly grounded. If the question were for de novo decision, the court would probably decide as he did. But it is enough to say his determinations are reasonable and rational.

Though they had ample opportunity to present anything pertinent to the FDA, plaintiffs urge that they should be permitted to make a new record here, presumably to show that the Commissioner must be denounced as

"arbitrary and capricious" on the basis of materials he was not invited to look at. The argument would appear to lack merit, but it need not be resolved finally for present purposes. Moving with the relative dispatch required by the occasion, the court has considered all the materials submitted, including those the Commissioner was not given. The result remains that the rationality of the questioned regulations unquestionably survives the effort to block them by a preliminary injunction.

The balance of the equities is heavily against the plaintiffs. They have offered some unimpressive figures for the expense of relabeling their vitamin bottles and putting up new pill strengths - for all of which the Commissioner gave long notice before the effective date of his regulations. Informed that the figures were vague and unenlightening, plaintiffs expanded the alleged numbers in a brief. The result remains less than imposing.

If people want 20,000 or 30,000 units of Vitamin A, they can dose themselves with two or three pills - or, better still, see a doctor first.

As the court has attempted to indicate, this sort of mild obstacle to the swallowing of toxic amounts seems compellingly sensible - a quality not necessarily objectionable for regulatory decisions.

In short, the public interest in health quite overwhelms the financial concerns plaintiffs urge.

Beyond that, the likelihood that plaintiffs will succeed in this action seems negligible.

There are, then, no grounds for, and powerful grounds against, a preliminary injunction.

Plaintiffs' motion is denied. So ordered.

Dated: New York, New York
September 25, 1973

Marvin E. Frankel
U.S.D.J.

UNITED STATES COURT OF APPEALS

FOR THE SECOND CIRCUIT

No. 439 - September Term, 1973

(Argued October 19, 1973 Decided November 2, 1973)

Docket No. 73-2430

THE NATIONAL NUTRITIONAL FOODS ASSOCIATION and SOLGAR CO., INC.,

Plaintiffs-Appellants,

v.

CASPAR W. WEINBERGER, Secretary of Health, Education and Welfare, and ALEXANDER M. SCHMIDT, Commissioner of Foods and Drugs,

Defendants-Appellees.

BEFORE:

MEDINA, LUMBARD and TIMBERS, Circuit Judges.

Appeal from an order entered in the Southern District of New York by Marvin E. Frankel, District Judge, which denied appellants' motion for a preliminary injunction to enjoin from becoming effective certain regulations of the Food and Drug Administration concerning Vitamins A and D.

Affirmed.

Milton A. Bass, New York, N.Y. (Bass & Ullman, New York, N.Y., on the brief), for plaintiffs-appellants.

Naomi L. Reice, Asst. U.S. Atty., New York, N.Y. (Paul J. Curran, U.S. Atty., and John W. Nields, Jr., Asst. U.S. Atty., on the brief), for defendants-appellees.

PER CURIAM:

The sole issue on this appeal from an order entered September 25, 1973 in the Southern District of New York by Marvin E. Frankel, District Judge, which denied plaintiffs' motion for a preliminary injunction to enjoin regulations of the Food and Drug Administration concerning Vitamins A and D from becoming effective, is whether, under the well established standards in this Circuit applicable to the extraordinary remedy of a preliminary injunction, the district court abused its discretion in denying it. We affirm.

Appellants are the National Nutritional Foods Association, a trade association of manufacturers, wholesalers and retailers of vitamins and dietary supplements, and Solgar, Co., Inc., a manufacturer, distributor and seller of vitamin supplements. Appellees are the Secretary of HEW and the Commissioner of Foods and Drugs.

On December 19, 1972, the Commissioner proposed, by publishing in the Federal Register, certain regulations of the Food and Drug Administration requiring that preparations of Vitamin A and Vitamin D in excess of 10,000 I.U. (international units) per dosage unit and 400 I.U. per dosage unit, respectively, be restricted to prescription sale and that such vitamins be labelled accordingly. 37 Fed. Reg. 26618 (1972), as amended, 38 Fed. Reg. 799 (1973). The regulations were proposed to implement the "efficient enforcement" of Sections 502(a), (f) and (j) and 503(b) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. §§352(a), (f) and (j) and 353(b)(1970), as authorized by 21 U.S.C. §371(a)(1970), and pursuant to powers delegated to the Commissioner by 21 C.F.R. §2.120(a)(1)(1973).

Consideration of the proposed regulations followed standard rule making procedure prescribed by the Administrative Procedure

Act, 5 U.S.C. §553 (1970), including requirements as to notice and public participation. Among the 2500 comments received in response to the Commissioner's invitation were comments from the two appellants herein, each of which submitted voluminous factual material and expert opinions opposing the proposed regulations. After due consideration, the Commissioner concluded that the regulations should be adopted. Accordingly, they were promulgated on July 25, 1973, to become effective October 1, 1973. 38 Fed. Reg. 20725, 20725 (1973).

Having failed to dissuade the Commissioner from promulgating the regulations, appellants on August 6, 1973 commenced the instant action in the Southern District of New York seeking declaratory and injunctive relief. Jurisdiction was invoked pursuant to 28 U.S.C. §1331(a) (1970). A week later, appellants filed their motion for a preliminary injunction which Judge Frankel denied on September 25, 1973 in an opinion setting forth his findings of fact and conclusions of law. On September 26, we ordered an expedited appeal and heard it on October 19.

Our careful examination of the record satisfies us that it fully supports the district court's denial of a preliminary injunction under the well established standards in this Circuit applicable to the extraordinary relief sought. See Gulf & Western Industries, Inc. v. Great Atlantic & Pacific Tea Company, Inc., 476 F.2d 687, 692-93 (2 Cir. 1973), and authorities there cited.

We affirm for the reasons stated in Judge Frankel's comprehensive opinion. ___ F.Supp. ___ (S.D.N.Y. 1973).

Affirmed.

NOTICE OF DEPOSITION
(Filed October 5, 1973)

350a

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

NATIONAL NUTRITIONAL FOODS ASSOCIATION and SOLGAR CO., INC.,

Plaintiffs,

vs.

CASPER W. WEINBERGER, Secretary of Health, Education & Welfare and ALEXANDER M. SCHMIDT, Commissioner of Food & Drugs,

Defendants.

73 Civ. 3448 (MEF)

NOTICE OF DEPOSITION UNDER F.R.C.P. 30(b)

S I R :

PLEASE TAKE NOTICE that pursuant to Rule 30(b) of the Federal Rules of Civil Procedure the deposition of defendant Alexander M. Schmidt, Commissioner of Food and Drugs and or such knowledgeable person or persons he may designate will be taken on oral examination at the offices of Bass & Ullman, Esqs., 342 Madison Avenue, New York, New York 10017, on Monday, October 15, 1973 at 10 o'clock A.M. and at any and all adjournments thereof.

The above named persons, whose depositions are being taken, are hereby notified to appear for said deposition and to bring with them any and all books, correspondence, records, medical reports and literature relating to their determination of the dosage levels of Vitamins A and D which are issue in the above entitled action.

Dated: New York, New York
October 5, 1973

Yours, etc.,

BASS & ULLMAN
Attorneys for Plaintiffs
Office & P.O. Address
342 Madison Avenue
New York, New York 10017
(212) 697-3880

TO: PAUL J. CURRAN, ESQ.
United States Attorney
Southern District of New York
Attorney for Defendants
United States Courthouse
Foley Square
New York, New York 10007

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

THE NATIONAL NUTRITIONAL FOODS ASSOCIATION, and SOLGAR CO., INC.,	:	
Plaintiffs,	:	
-against-	:	TEMPORARY RESTRAINING ORDER AND ORDER TO SHOW CAUSE
CASPAR W. WEINBERGER, Secretary of Health, Education and Welfare, and ALEXANDER M. SCHMIDT, Commissioner of Food and Drugs,	:	73 Civ. 3448 (MEF)
Defendants.	:	

Upon the annexed affidavit of Naomi L. Reice, Assistant United States Attorney, sworn to on October 11, 1973, and the exhibit attached hereto, it is hereby

ORDERED, that the plaintiffs, The National Nutritional Foods Association and Solgar Co., Inc., show cause before the Honorable Marvin E. Frankel, a Judge of this Court, at the United States Courthouse, Foley Square, New York, New York, in Room 2002, on the _____day of October, 1973, at _____o'clock in the _____noon, or as soon thereafter as counsel may be heard, why an order should not be entered pursuant to Rule 26(c) of the Federal Rules of Civil Procedure, vacating a notice of deposition directed to defendant Alexander M. Schmidt or his designee which plaintiffs have served upon defendants' attorney; and

it is

ORDERED, that the plaintiffs are hereby restrained from taking the depcsition of defendant Alexander M. Schmidt or his designee pending the hearing upon defendants' motion for a protective order; and it is further

ORDERED, that a copy of this order and all papers upon which it is based shall be served upon the office of the attorney for the plaintiffs on or before the _____day of October, 1973, at _____M.

Dated: New York, New York

October , 1973

United States District Judge

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

THE NATIONAL NUTRITIONAL FOODS ASSOCIATION and SOLAR CO., INC.,

Plaintiffs,

-against-

CASPAR W. WEINBERGER, Secretary of Health, Education and Welfare, and ALEXANDER M. SCHMIDT, Commissioner of Food and Drugs,

Defendants.

AFFIDAVIT

73 Civ. 3448 (MEF)

STATE OF NEW YORK)
COUNTY OF NEW YORK : ss.:
SOUTHERN DISTRICT OF NEW YORK)

NAOMI L. REICE, being duly sworn, deposes and says:

1. I am an Assistant United States Attorney in the office of Paul J. Curran, United States Attorney for the Southern District of New York, attorney for the defendant Alexander M. Schmidt, Commissioner of Food and Drugs, and as such I am in charge of and familiar with this action.

2. I make this affidavit in support of defendants' application for an order directing the plaintiffs in the action to show cause why an order should not be entered vacating a notice to take the deposition of defendant Schmidt or his designee which plaintiffs have served upon defendant's attorney. A copy of that notice is annexed

hereto as Exhibit A.

3. Defendants make this motion because in an action such as this, in which plaintiffs seek declaratory and injunctive relief to prevent the enforcement of duly issued regulations of an administrative agency, the Administrative Procedure Act and the cases thereunder (which were cited by defendants in their Memorandum in Opposition to plaintiffs' Motion for a Preliminary Injunction, filed on September 10, 1973, at pages 18-19) directs that a court's review be based upon the administrative record. That administrative record has already been filed with this Court. Litigation affidavits, and likewise deposition testimony, are not part of the whole record to which the Administrative Procedure Act focuses the Court's attention. Accordingly, we submit that, in the absence of highly special or unusual circumstances which might make depositions appropriate in a case such as this, there are no matters relevant to this case which could be inquired into on deposition. The taking of Mr. Schmidt's deposition in these circumstances would be unduly burdensome and oppressive.

4. The reason why this application is made by order to show cause rather than ordinary notice of motion is that an ordinary motion would be returnable after the date noticed for the taking of Mr. Schmidt's deposition.

5. No prior application has been made for the relief requested herein.

WHEREFORE, your deponent respectfully requests that the order to show cause in support of which this affidavit has been submitted be signed and entered by this Court.

/s/
NAOMI L. REICE
Assistant United States Attorney

Sworn to before me this
11th day of October, 1973

Notary Public

WALTER G. BRANNON
Notary Public, State of New York
No. 24-0394500
Qualified in Kings County
Cert. filed in New York County
Term Expires March 30, 1975

6. At 3:25 P.M., I spoke to Melton Bass, Esq. counsel to plaintiffs and informed him of this order to show cause and its stay provision. Mr. Bass consented to the stay contained herein and requested that the motion be made returnable during the week of October 22, 1973, subsequent to oral argument before the Court of Appeals in this matter on October 19, 1973

NLR

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

(Filed October 25, 1973)

THE NATIONAL NUTRITIONAL FOODS ASSOCIATION and SOLGAR CO., INC.,

Plaintiffs,

-against-

CASPER W. WEINBERGER, Secretary of Health, Education and Welfare, and ALEXANDER M. SCHMIDT, Commissioner of Food and Drugs,

Defendants.

73 Civ. 3448 (MEF)

AFFIDAVIT IN OPPOSITION TO DEFENDANTS' MOTION

STATE OF NEW YORK)
) SS.:
COUNTY OF NEW YORK)

MILTON A. BASS, being duly sworn, deposes and says:

I am a member of the firm of Bass & Ullman, attorneys for the plaintiffs herein and respectfully submit this affidavit in opposition to defendants' motion to vacate the notice of deposition directed to defendant Alexander M. Schmidt.

The defendants seek to vacate the notice of deposition of Alexander M. Schmidt on the ground that the court's review in the instant action is limited to the administrative record herein. The briefs of both parties have heretofore been submitted to the Court with respect to this question of law. At this time, plaintiffs merely wish to add that the basic issue, which is presented upon this motion and upon the defendants' motion to dismiss, is really a very narrow one. If the defendants had filed a complaint and instituted an action claiming that a product was covered by the prescription statute, then, and in such

event the defendants would have had to go forward and prove their case by proper and relevant evidence. The defendants are here arguing that merely by issuing an interpretive regulation they no longer have to meet this burden.

No hearing was ever conducted by the Agency. The Agency merely invited comments about its proposed regulation. The defendants have argued that they did not even have to invite comments for the purpose of issuing an interpretive regulation. The argument of the defendants is simply that they merely have to issue an interpretive regulation stating that a product is covered by the prescription statute and that automatically becomes the law without any right to a trial, including cross-examination of the defendants' witnesses.

The defendants' contention is most certainly a new and unique interpretation of the law and of due process. If the defendants are correct, they will no longer have to bring actions claiming violations of the statute, but need merely issue interpretive regulations. Plaintiffs respectfully submit that the defendants are in error.

For the reasons herein set forth and as set forth in plaintiffs' briefs heretofore submitted to the Court, it is respectfully submitted that the defendants' motion should be denied.

s/ MILDRED A. BASS

Sworn to before me this

day of October, 1973.

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

THE NATIONAL NUTRITIONAL FOODS ASSOCIATION and SOLGAR CO., INC.,

Plaintiffs,

-against-

CASPER W. WEINBERGER, Secretary of Health, Education and Welfare, and ALEXANDER M. SCHMIDT, Commissioner of Food and Drugs,

Defendants.

73 Civ. 3448 (MEW)

SUPPLEMENTAL AFFIDAVIT IN OPPOSITION TO DEFENDANTS' MOTION TO VACATE NOTICE OF DEPOSITION.

STATE OF NEW YORK)
) ss.:
COUNTY OF NEW YORK)

MILTON A. BASS, being duly sworn, deposes and says:

1. I am a member of the firm of Bass & Ullman, attorneys for plaintiffs and I make this supplemental affidavit in opposition to the motion brought on by defendants by way of an order to show cause requesting this Court to vacate a notice of deposition served by plaintiffs.

2. On October 5, 1973, plaintiffs served a notice of the taking of the deposition of Alexander M. Schmidt, Commissioner of Food and Drugs or his knowledgeable designee, along with a request for the production of all relevant documents, for the purpose of determining the basis for the dosage levels established in the Vitamin A and D regulations. Defendants' motion to vacate said notice is based on their contention that this Court is limited to reviewing the administrative "record" filed by the

Food and Drug Administration for the purpose of determining whether the action of the Commissioner was "arbitrary and capricious." 5 U.S.C. §706(2)(A). The instant case involves consideration of a "policy statement" or interpretive regulation issued by the defendants. There has never been a hearing in this matter, nor has there been any opportunity for cross-examination of witnesses.

3. Plaintiffs contend that the defendants cannot accomplish a restriction on the scope of review by issuing an interpretive regulation or policy statement instead of proceeding by way of a seizure or injunction action as contemplated by the Federal Food, Drug, and Cosmetic Act. It is important to note that prior to the landmark decision in the Abbott Laboratories case such regulations and policy statements were not subject to pre-enforcement judicial review. Instead, they could only be challenged when and if an administrative agency sought to enforce such regulation or policy statement by way of a criminal or civil proceeding. In such proceedings, the administrative agency would have had the full burden of establishing the validity of their policy statement or interpretive regulation and the defendant would have had a full opportunity to cross-examine the agency witnesses and to present his own proof.

The decision in Abbott Laboratories held that the federal courts do have jurisdiction to entertain an action for a declaratory judgment for pre-enforcement relief. Thus, after the Food and Drug Administration issues a statement of policy or interpretive regulation, an affected party no longer has to await

and risk the hazards of a seizure or injunction action in order to obtain judicial relief. Instead, they can, as have the plaintiffs in the instant case, bring an action for declaratory judgment anticipating enforcement by the agency for the purpose of obtaining a judicial determination as to the validity of the agency action. The Court in Abbott Laboratories did not change the law as to the burden of proof and the scope of judicial review.

By seeking to limit the scope of review by this Court, defendants are in effect proposing a new rule of law contrary to the specific legislative history of the prescription statute and destructive of basic principles of due process, as well as a frustration of the legitimate purpose of a declaratory judgment action.

4. Even if the Court adopts the new rule of law proposed by defendants as to the scope of review, plaintiffs respectfully submit that discovery proceedings are nevertheless appropriate and essential in the instant case. The Administrative Procedure Act expressly states:

> "In making the...determinations, the court shall review the whole record...." 5 U.S.C. §706 (emphasis added)

This requirement relates to a full review by the Court of the entire record on which the administrative agency based its decision. Anything less than the "whole record" is not sufficient for a proper decision as to the propriety of the action taken by the administrative agency.

5. Plaintiffs respectfully submit that the record filed by the Food and Drug Administration in this case is not the "whole record" which was before the agency in that there are,

at least, the following substantial omissions and inadequacies:

A. The regulations establish prescription limitations at levels of 10,000 I.U. and 400 I.U. for Vitamins A and D respectively. The record does not show how these levels were determined. The only support for the levels are conclusory statements without any explanation or analysis. There have been no findings that any specific level of Vitamins A or D are toxic or have potentiality for harmful effect. Discovery is essential to ascertain the basis, if any, for the dosage levels established by defendants.

B. In his policy statement, the Commissioner makes the following statement:

> "Based on consultation with the most knowledgeable experts available, the Commissioner finds that the scientific consensus is that the proposed limits are appropriate at this time." 38 F.R. 20724, col. 2 (Aug. 2, 1973) (emphasis added)

None of these consultations are part of the record in this Court. There is no indication as to who these "most knowledgeable experts" are and there is nothing in the record which states the substance of their communications to the Commissioner. Discovery is most certainly essentdal to ascertain these facts which defendant expressly states comprised the basis for his decision.

C. The Commissioner relies on a bibliography of articles in the medical literature to support the

Vitamin A and D regulations. 37 F.R. 26618 (Dec. 14, 1972). He states that several comments submitted made "their own analysis of the bibliography." 38 F.R. 20724 (Aug. 2, 1973). There is nothing in the record which presents the analysis of the bibliography, if any, which was made by the Food and Drug Administration in connection with determining the levels established for Vitamins A and D. There has been no opportunity for cross-examination of witnesses to ascertain what scientific conclusions can properly be drawn from this bibliography.

D. The Commissioner states that above the levels specified in the regulations, Vitamins A and D are appropriate only for therapeutic purposes. 38 F.R. 20723, col. 3 (Aug. 2, 1973). This contention is essential for the Commissioner's position that the products are drugs. The record does not show what the therapeutic purposes for Vitamins A and D are above the levels set, nor how the Commissioner decided that such therapeutic purposes exist.

The Commissioner bases a finding that Vitamins A and D have no food value above 10,000 I.U. and 400 I.U. on other regulations promulgated by him in another context. 38 F.R. 20723, col. 1 (Aug. 2, 1973). These regulations were promulgated after a two year public hearing and the factual and legal conclusions in them are currently being challenged in the

Court of Appeals for the Second Circuit. As a result of this challenge, the Food and Drug Administration stayed the effectiveness of those regulations. 38 F.R. 29577 (Oct. 26, 1973). No part of the record in the other regulations is part of the record filed by the FDA in this Court. There is nothing in the record herein to support a factual determination that Vitamins A and D have no food value at the specified dosage levels.

E. In his policy statement, the Commissioner makes the following statement:

> "The margins of safety provided in the levels established by this proposal were developed to take into account the wide ranges of vitamin content in foods and the dosage levels of Vitamin A & D that are usually implicated in toxic conditions." 38 F.R. 20724, cols. 2-3 (Aug. 2, 1973).

There is nothing in the record herein which shows how this formulation of a margin of safety was accomplished.

F. In his policy statement, the Commissioner makes the following statement:

> "Comment was received that consumers would be able to ingest as many dosage units as they desired and therefore the proposed limits would have no effect. The Commissioner cannot agree with this concept. The Commissioner believes that most consumers will carefully consider the advisability of taking dosages in excess of suitable recommended dosages. Conscientious consumers will have a basis upon which to make a judgment as to their intake of these vitamins. The fact that a small

> number of consumers will abuse their health...is no reason to forego a reasonable regulation that will afford appropriate public health protection for the vast majority of the public." 38 F.R. 20725, col. 3 (Aug. 2, 1973).

This issue relates to the purpose of the prescription requirement for a product and similarly requires adequate cross-examination for proper review in this Court.

G. The Food and Drug Administration previously issued a notice in which they took the position that Vitamins A and D in dosages of 50,000 I.U. each were subject to a prescription requirement. 36 F.R. 16125 (Aug. 19, 1971). There is nothing in the record to explain what new information was received by the FDA to justify the drastic reduction from the earlier levels they attempted to establish.

H. Although the Commissioner recognizes a distinction between children and adults with respect to toxicity levels [37 F.R. 26619, col. 1 (Dec. 14, 1972)], the record is silent as to why the regulations do not contain such a distinction. See 38 F.R. 20724, col. 1 (Aug. 2, 1973) where the Commissioner notes but does not respond to this objection as to non-distinction between children and adults.

I. Under the statute there are two requirements for placing a drug on a prescription basis:

1. The product must be toxic or have a potentiality for harmful effect, and

2. As a result of the above it must not be safe for use except under the supervision of a physician.

See 21 U.S.C. §353(b)(2)(B)

There is nothing in the record to explain how the Commissioner determined that the second of the above requirements was complied with and that Vitamins A and D at the specified levels were not safe for use except under the supervision of a physician.

6. In support of the Vitamin A and D regulations, the defendant has referred to a series of articles and reports. No findings or statements have been made as to the scientific conclusions which can be drawn from those articles. Cross-examination is most essential in this area. We must ascertain what scientific and factual conclusions were made by the Commissioner as a result of his review of this literature and whether these conclusions properly support the Vitamin A and D regulations. This is particularly significant in the instant case since no findings have been made or even attempted with respect to ascertaining the purported levels of toxicity for Vitamins A and D.

7. Plaintiffs respectfully submit that the discovery sought by their notice of deposition is necessary and proper for a determination of whether the Commissioner acted reasonably in promulgating the Vitamin A and D regulations. If, for example, the defendants cannot furnish a proper basis for arriving at the levels specified in the regulations, surely the regulations would have to be considered arbitrary. If, on the other hand, a proper

formulation of these levels was made, there can be no legitimate reason for attempting to prevent disclosure of the scientific basis for the defendants' decision on these regulations.

8. The omissions and inadequacies in the record referred to above, frustrate the proper scope of review by this Court even under the limited theory proposed by defendants. It is, therefore, respectfully submitted that full access to discovery procedures is necessary herein in order to enable this Court to review the action of the defendant upon all of the factors and information which were before the administrative agency. Consequently, defendants' motion to vacate the notice of deposition should be denied.

MILTON A. BASS

Sworn to before me this
26th day of December, 1973.

JACOB LAUFER
NOTARY PUBLIC, State of New York
No. 31-4502285
Qualified in New York County
Commission Expires Mar

NLR:lw
73-2562

AFFIDAVIT OF NAOMI L. REICE WITH AFFIDAVIT OF STEPHEN MC MAMARA ANNEXED

UNITED STATES DISTRICT COURT (Filed December 13, 1973)
SOUTHERN DISTRICT OF NEW YORK

THE NATIONAL NUTRITIONAL FOODS ASSOCIATION and SCHAR CO., INC.,

Plaintiffs,

-against-

CASPAR W. WEINBERGER, Secretary of Health, Education and Welfare, and ALEXANDER M. SCHMIDT, Commissioner of Food and Drugs,

Defendants.

73 Civ. 3448 MC

STATE OF NEW YORK)
COUNTY OF NEW YORK : ss.:
SOUTHERN DISTRICT OF NEW YORK)

NAOMI L. REICE, being duly sworn, deposes and says:

I am an Assistant United States Attorney in the office of Paul J. Curran, United States Attorney for the Southern District of New York, attorney for the defendants herein. This affidavit accompanies the affidavit of Stephen H. McNamara and the exhibits therewith. The exhibits to the affidavit of Mr. McNamara, which are copies of the medical articles referred to in the bibliography included in the record already on file with the Court, are provided for the convenience of the Court if the Court deems necessary further material when ruling upon the outstanding motions before it and any additional matters that may arise.

s/
NAOMI L. REICE
Assistant United States Attorney

Sworn to before me this
13th day of December, 1973.

s/
MARY L. A[illegible]
Notary Public

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK
----------X

THE NATIONAL NUTRITIONAL FOODS ASSOCIATION and SOLGAR CO., INC.,

Plaintiffs,

against

CASPAR W. WEINBERGER, Secretary of Health, Education, and Welfare, and ALEXANDER M. SCHMIDT, Commissioner of Food and Drugs,

Defendants.

73 Civ. 3448

AFFIDAVIT

----------X

County of Montgomery)
State of Maryland) ss

Stephen H. McNamara, being first duly sworn, deposes and says:

I am an attorney employed by the United States Department of Health, Education, and Welfare, Office of the General Counsel, Food and Drug Division, which provides legal services to the United States Food and Drug Administration.

When the Commissioner of Food and Drugs promulgated the Notice of Proposed Rulemaking concerning prescription status for high dosages of vitamins A and D in the Federal Register of December 14, 1972 (37 F.R. 26618), a listing of a number of pertinent articles regarding these vitamins was placed on file with the Hearing Clerk for public view and use in commenting on the proposal. (The public availability of this listing was announced in the Notice of Proposed Rulemaking. A copy of the listing should appear in volume one of the copy of the record which is already on file with the Court.)

Many of the comments, including the comment filed by plaintiff National Nutritional Foods Association, discussed the contents of these articles.

The articles themselves were not placed on display since they had been published in various medical journals and the citations are sufficient for securing copies of the articles in medical libraries. (Such citation is the medical analog of the legal custom of citing

published judicial decisions, legal articles, etc., in briefs, etc. without attaching copies.) Pursuant to my request, the Bureau of Drugs Library has assembled copies of the articles, which accompany this Affidavit, for the Court's reference in this case.

Stephen H. McNamara

Stephen H. McNamara

Subscribed and sworn to before me this 9th day of November, 1973, in the County and State aforesaid.

Francis E. McKay

Notary Public

MY COMMISSION EXPIRES
JULY 1, 1974

OPINION OF DISTRICT COURT VACATING NOTICE OF DEPOSITION AND DISMISSING COMPLAINT

UNITED STATES DISTRICT COURT (Filed April 5, 1974)
SOUTHERN DISTRICT OF NEW YORK

- x

THE NATIONAL NUTRITIONAL FOODS ASSOCIATION AND SOLGAR CO., INC.,

Plaintiffs,

-against-

CASPAR W. WEINBERGER, Secretary of Health, Education and Welfare, and ALEXANDER M. SCHMIDT, Commissioner of Food and Drugs,

Defendants.

73 Civ. 3448

OPINION

- x

A P P E A R A N C E S :

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Paul J. Curran, United States Attorney
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Naomi L. Reice, Assistant United States Attorney
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FRANKEL, D.J.

On October 1, 1973, regulations of the Food and Drug Administration became effective requiring that preparations of Vitamin A and Vitamin D in excess of 10,000 IU

(international units) per dosage unit and 400 IU per dosage unit, respectively, be restricted to prescription sale and that such vitamins be labeled accordingly. 21 C.F.R. §§3.94 and 3.95 (1973). The regulations were declared to have been promulgated to implement the "efficient enforcement" of §§502(a), (f), and (j) and 503(b) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. §§352(a), (f), and (j) and 353(b), under the general authority of the Act's §701(a), 21 U.S.C. §371(a), and pursuant to powers delegated to the Commissioner by 21 C.F.R. §2.120(a)(1)(1973).

Plaintiffs, involved in the manufacture, distribution, and sale of Vitamins A and D, filed suit on August 6, 1973, seeking declaratory and injunctive relief against the regulations. Their motion for a preliminary injunction was denied on September 25, 1973. National Nutritional Foods Ass'n v. Weinberger, 366 F.Supp. 1341, aff'd Docket No. 73-2430 (2d Cir., December 11, 1973).

Defendants have now moved for summary judgment dismissing the complaint. Counsel have made extensive submissions, and the court has heard further oral argument, supplementing the things read and heard on the motion for a

preliminary injunction. For reasons hereinafter outlined, the complaint is now to be dismissed.

I.

Plaintiffs claim that the questioned regulations were issued by the Commissioner without statutory authority. They argue that the legislative history of the prescription drug statute, 21 U.S.C. §353(b)(1)[1] reveals a purpose to prohibit regulations of this kind. The history shows, plaintiffs say, that the prescription requirement was meant to be for case-by-case determination in court, not for administrative rules like those before us. This intended limitation, they argue, may not be surmounted or avoided by the more general authority of the Commissioner to issue regulations under 21 U.S.C. §371(a). These contentions have substance. Having considered them, however, the court concludes that the legislative history is by no means clear enough to preclude a look at the statutory text,[2] and that the legislative mandate as a whole sustains the agency's position.

The Food, Drug and Cosmetic Act (the Copeland Act), 21 U.S.C. §301 et seq., was passed in 1938, superseding a 1906 statute touching the subject (the Wiley Act, c. 3915, 34 Stat. 768). The new Act was designed to respond to "profound changes in methods of manufacturing and selling foods and drugs" which had developed since 1906 and to remedy "textual weaknesses in the measure that were not foreseen when it was enacted." 79 Cong. Rec. 4758 (remarks of Sen. Copeland); see generally Jackson, Food and Drug Legislation in the New Deal (1970). Section 503(b) of the Act, 21 U.S.C. §353(b) (the prescription drug statute), was further amended in 1951 by the Durham-Humphrey Amendment, c. 578, 65 Stat. 648 (1951). This amendment and its history are the central subjects of plaintiffs' case.

The general purpose of the 1951 legislation was to adapt the Food, Drug and Cosmetic Act—

> "to deal realistically with the labelling and dispensing of drugs that may be sold only upon the prescription of licensed practitioners. Its provisions are remedial in the sense that they are intended to protect the public from abuses in the sale of potent prescription medicines. They will also relieve retail pharmacists of unnecessary restrictions in the dispensing of drugs that are safe for use without medical

supervision." S. Rep. No. 946, 82d Cong., 1st Sess. cited in 1951 U.S.Code Cong. and Admin. News 2454.

Accordingly, the amended section 503 created a new prescription requirement encompassing a statutory definition of drugs that may be dispensed only on prescription and specifying the conditions under which these drugs may be dispensed. Before, the law had simply commanded that the labeling of drugs bear adequate directions for use. While the Commission had provided some regulatory suasion,[3] it had been for the drug manufacturer to make the primary determination as to whether a prescription was necessary; the resulting lack of uniformity had left the retail druggist adrift in identifying his statutory (and health) obligations. One manufacturer might determine that a prescription legend was required for the same drug that a competing manufacturer considered suitable for over-the-counter sale. See H.R. Rep. No. 700, 82d Cong., 1st. Sess.3 (1951). As originally proposed, in H.R. 3298, the amended §503(b) would have conferred authority on the F.D.A. to issue an administrative list of drugs requiring prescription

prior to sale. While this provision was opposed by many drug manufacturers, it remained in the bill as reported out by the House Committee on Interstate and Foreign Commerce. Among the considerations which influenced the Committee in its decision to retain this aspect of the bill was the recognition that "the task of determining which drugs shall be sold only on prescription is, in its nature, essentially a legislative or rule-making function, unsuited for solution solely through the judicial process." H.R. Rep. No. 700, supra at 10.

A minority report asserted that "the present method which leaves this determination [of whether a prescription is required] to the courts, should be left unchanged except that a proper standard to be applied in determining whether a drug is dangerous should be incorporated in the statute." Id. at 28. The minority argued that providing the Administrator with power to issue regulations was a "dangerous delegation of authority" which would "add to present difficulties by increased bureaucratic regulation." Id.

H.R. 3298 reached the floor of the House on July 31, 1951, 97 Cong. Rec. 9235 (1951). The minority

view on handling the prescription requirement gathered support, on stated grounds both of general principle and of specific hostility to the then Administrator. On August 1, Congressman O'Hara of Minnesota introduced an amendment to strike the sections of the bill providing for the promulgation of an administrative list of drugs requiring a prescription for sale. The amendment carried. In its amended form H.R. 3298 was passed by the House and sent to the Senate, where it was reported out favorably and passed with minor amendments (and no significant debate) on October 15, 1951.

The Senate Committee which considered H.R. 3298 as passed by the House had before it both H.R. 3298 and a companion Senate bill, S. 1186 with various amendments in the nature of a substitute by Senator Humphrey designed to reintroduce the administrative list. While the Committee ultimately accepted the House version, it noted that the statutory definition simpliciter would be difficult or impossible to administer. The Committee Report explicitly contemplated the formulation of implementing regulations under 21 U.S.C. §371(a) to effectuate the statutory objective of protecting the public

health:

"In order to give this general definition a more precise meaning so that it may be applied with greater uniformity by the drug trade the Administrator can exercise the authority he has under section 701(a) of the Federal Food, Drug, and Cosmetic Act to issue interpretative regulations. It is to be understood that the inclusion of the statutory definition does not, of course, in any way derogate from the Administrator's authority to interpret and enforce the definition through the issuance of any regulations necessary or appropriate to protect the public from indiscriminate dispensing of drugs over the counter when they may be unsafe for use without the supervision of a practitioner licensed by law to administer such drugs.

"As previously stated, the committee considered S. 1186 together with H.R. 3298. S. 1186 would have authorized the Federal Security Administrator to list by name or class the drugs which he considered within the statutory definition. The grant of such administrative authority was objected to as an unnecessary regulation of the drug industry, and the committee concluded that administrative listing is not necessary at this time. It was felt that the statutory definition, together with the authority to make interpretative regulations, could bring an end to the existing confusion in drug labeling and that uniformity can be achieved through cooperative efforts of the drug industry and the Food and Drug Administration working under the statutory plan. If the present confusion is not ended by this legislation it will then be time enough to consider the need for the administrative listing approach.

* * *

> "Furthermore, in determining whether a drug is safe for use without medical supervision, there must be taken into consideration not only the drug's toxicity, but also other potentialities for harmful effect, the method by which it is used and the collateral measures necessary to its safe use. The broad language of the definition contained in this subparagraph is intended to comprehend all drugs that in fact should be administered under medical supervision in order to insure their safe use. Such difficult borderline cases as may arise under this definition can be dealt with under the interpretative and rule-making power provided for in section 701(a) of the act." S. Rep. No. 946, 82d Cong., 1st Sess., cited in 1951 U.S. Code Cong. and Admin. News 2457, 2462 (emphasis added).

In these expressions at least, there was a plain understanding that whatever specific rule-making powers were given to the F.D.A., the Commissioner would be required and expected to use his §701(a) power "to promulgate regulations for the efficient enforcement of this Act" in making the prescription requirement effective. As for the House, if it rejected the broad project of an "administrative list," it left §701(a) intact and nowhere indicated a purpose to render that section inoperative for purposes of the new prescription provision.[4]

Wherever the legislative history alone might leave us, the Commissioner's position finds solid support in §701(a) of the Act, 21 U.S.C. §371(a), and judicial as well as administrative constructions of this provision. Section 701(a) empowers the Commissioner, as delegee of the Secretary of Health, Education and Welfare, 21 C.F.R. §2.120 (1973), "to promulgate regulations for the efficient enforcement of" the Act, including the Act's prescription requirement in §353(b). Plaintiffs argue this is authority for mere "housekeeping" provisions, and they contrast subsection (e)[5] with subsection(a) of §701 to buttress the argument.[6] But the contention is not only at war with a considerable body of administrative practice;[7] it is also contrary to controlling judicial authority. Weinberger v. Hynson, Westcott & Dunning, 412 U.S. 609 (1973), sustained the F.D.A's authority under §701(a) to create an "administrative summary judgment procedure" (p. 617) having the drastic consequence, in cases to which it applied, of withdrawing approval of new drug applications without an evidentiary hearing. The administrative action was upheld as a valid instance of "particularizing standards through the

rulemaking process,"[8] deemed necessary and proper to prevent the "paralysis" of the administrative process which "would result if case-by-case battles in the courts were the only way to protect the public against unsafe or ineffective drugs." P. 626. Equally enlightening, if not technically "square" authority, is the pronouncement in Weinberger v. Bentex Pharmaceuticals, Inc., 412 U.S. 645, 653 (1973), that the agency's power to determine "new drug" status in its own administrative proceedings was "implicit in the regulatory scheme" though "not spelled out in haec verba . . . ." Again, the construction was powerfully influenced by the recognition that a different view "would seriously impair FDA's ability to discharge the responsibilities placed on it by Congress." CIBA Corp. v. Weinberger, 412 U.S. 640, 643 (1973).

Our Court of Appeals has recognized similarly that "the Commissioner has the power to issue binding interpretative regulations," citing to another example of the authority sustained under §701(a), Abbott Laboratories v. Gardner, 387 U.S. 136 (1967), and observing that "the particularization of a statute by rule-making is not only acceptable in lieu of protracted piecemeal

litigation . . . but is the preferred procedure. . . ." CIBA-Geigy Corporation v. Richardson, 446 F.2d 446, 468 (1971). This principle, applied in the instant case, implements our duty to treat the statute, with its paramount concern for life and health, "as a working instrument of government and not merely as a collection of English words." United States v. Dotterweich, 320 U.S. 277, 280 (1943); see also United States v. Bacto-Unidisk, 394 U.S. 784, 798 (1969); United States v. Sullivan, 332 U.S. 689, 696 (1948); Permian Basin Area Rate Cases, 390 U.S. 747, 776 (1968). The recent approval of legislative rulemaking power under a section of the Truth In Lending Act very like §701(a) in language, Mourning v. Family Publications Service, Inc., 411 U.S. 356, 369 (1973), adds further support to the Commissioner's position here, as does the D.C. Circuit's determination that the Federal Trade Commission possesses substantive rulemaking power although the statute does not explicitly say so. National Petroleum Refiners Association v. F.T.C., 482 F.2d 672, 676-677, 689-91 (D.C. Cir. 1973), pet. for cert. filed, 42 U.S.L.W. 3376 (U.S. Nov. 20, 1973) (No. 806).

If the foregoing citations do not dictate mechanically the result herein, they point the clear path to decision. The "case-by-case battles in the courts" deemed compulsory by plaintiffs would have to be borne if the law required them. The result would be, of course, a rickety apparatus of non-regulation, with judges making disparate and uninformed decisions about when prescriptions should or should not be required. Such de novo court hearings could in no way inure "to [those] interests of the public that Congress was anxious to protect," Weinberger v. Bentex Pharmaceuticals, et al., 412 U.S. 645, 653 (1973). It seems fortunate that the Act, read sensibly and as a whole, requires no such unhappy interpretation.

II.

Plaintiffs contend that they should have a de novo "trial," preceded by considerable discovery, to test the questioned regulations. There is no warrant for such explorations or for an evidentiary hearing of any kind. The agency was not required to hold a trial-type hearing before issuing its regulations, and none is either required or permitted in the court. It is sufficient

that the public, including the plaintiffs, were "given a significant opportunity prior to promulgation of . . . [the] . . . rule[s] to ventilate the policy and empirical issues at stake through written submissions." National Petroleum Refiners Association v. Federal Trade Comm., 482 F.2d 672, 693 (D.C. Cir. 1973), pet. for cert. filed, 42 U.S.L.W. 3376 (U.S. Nov. 20, 1973) (No. 806). Unlike the rare cases in which the absence of an administrative record may require the taking of evidence in court, e.g., Citizens to Preserve Overton Park v. Volpe, 401 U.S. 402, 419-420 (1971), there is a voluminous and unstinting record here. Some 46 volumes in size, "it consists of the submissions made in response to the invitations issued for written comments." Automotive Parts & Accessories v. Boyd, 407 F.2d 330, 331 (D.C. Cir. 1968). Plaintiffs had full opportunity to present everything they thought germane. The agency, referring to the extensive materials it received, has sufficiently "articulate[d] its bases and purposes" in promulgating the regulations. Buckeye Power v. EPA, 481 F.2d 162, 170-71 (6th Cir. 1973);

see also Associated Indus. of N.Y.S. Inc. v. Dept. of L., 487 F.2d 342, 354 (2d Cir. 1973); Mobil Oil Corporation v. Federal Power Commission, 469 F. 2d 130, 140 (D.C. Cir. 1972), cert. den., 412 U.S. 931 (1973); International Engineering Company v. Richardson, 361 F.Supp. 818, 823-25 (D.D.C. 1973).

In rulemaking of this sort, where the regulations must stand unless they are deemed irrational or arbitrary and capricious, Associated Indus. of N.Y.S. Inc. v. Dept. of L., 487 F.2d 342, 348 (2d Cir. 1973); Bunny Bear, Inc. v. Peterson, 473 F.2d 1002, 1005-06 (1st Cir. 1973); Unimed, Inc. v. Richardson, 458 F.2d 787, 789 (D.C. Cir. 1972); Boating Industry Association v. Boyd, 409 F.2d 408, 411 (7th Cir. 1969); Citizens Band Association v. United States, 375 F.2d 43, 53-54 (9th Cir. 1967), it would be "sufficient that the regulations be supported by evidence in [the Commissioner's] files, or even by [his] experience." Consumers Union of United States, Inc. v. Consumer Product Safety Commission, No. 73-1617, slip op. at 1150 (2d Cir. Jan. 4, 1974). The case

against plaintiffs is far stronger; in this domain of medical judgment, where certainty is not attainable and special caution to safeguard health is compelled, the prudent and easily managed restrictions the Commissioner has required are solidly supported by the materials that were before him and have been lodged with the court.

In any case it is clear that the main, if not the exclusive, object plaintiffs pursue is an exploration of the mental processes by which the Commissioner reached his results. Such explorations are rarely to be countenanced. United States v. Morgan, 313 U.S. 409, 422 (1941); see also National Nutritional Foods Association v. Food and Drug Administration, No. 73-2129 (2d Cir. Feb. 1, 1974), especially when, as here, the Commissioner's rationale is sufficiently articulated to allow for meaningful judicial review. Citizens to Preserve Overton Park v. Volpe, 401 U.S. 402, 420 (1971). No showing has been made to justify the extraordinary inquiry plaintiffs propose.

It is abundantly clear, then, that the court should, and it does, vacate plaintiffs' notice to depose defendant Commissioner or his designees at an examination to which deponents would be required to bring "any and all books, correspondence, records, medical reports and literature relating to their determination of the dosage levels of Vitamins A and D which are in issue . . . ." In sum, there are no factual issues to be tried. The administrative record was properly made. It is in no pertinent sense incomplete. It leads, as has been stated, to a ruling that the regulations are by no means arbitrary, capricious, or otherwise infirm. In so holding, the court has reconsidered the propositions of law underlying the denial of a preliminary injunction. Those premises are now adhered to and reaffirmed.

Plaintiffs' notice of deposition is vacated. Defendants' motion for summary judgment is granted. The complaint is dismissed.

So ordered.

Dated: New York, New York
April 5, 1974

Marvin E. Frankel
U.S.D.J.

FOOTNOTES:

1.

"(b)(1) A drug intended for use by man which—

" (A) is a habit-forming drug to which section 352(d) of this title applies; or

"(B) because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, is not safe for use except under the supervision of a practitioner licensed by law to administer such drug; or

"(C) is limited by an approved application under section 355 of this title to use under the professional supervision of a practitioner licensed by law to administer such drug,

shall be dispensed only (i) upon a written prescription of a practitioner licensed by law to administer such drug, or (ii) upon an oral prescription of such practitioner which is reduced promptly to writing and filed by the pharmacist, or (iii) by refilling any such written or oral prescription if such refilling is authorized by the prescriber either in the original prescription or by oral order which is reduced promptly to writing and filed by the pharmacist. The act of dispensing a drug contrary to the provisions of this paragraph shall be deemed to be an act which results in the drug being misbranded while held for sale."

2. See Greenwood v. United States, 350 U.S. 366,374 (1956) (Frankfurter, J.).

3. In 1944, the F.D.A. promulgated regulations designed to provide some guidance as to what drugs would be exempted from various warning requirements on their labels if only prescription sale was allowed. These standards were similar to those later incorporated in the Durham-Humphrey Amendment. See 21 C.F.R. §1.106 (b)(1) and (b)(2) (ii)(1949.

4. Contemporary trade circles recognized that this would be the case as well. See Dunn, The New Prescription Drug Law, 6 Food, Drug, Cosm. L.J. 951, 955-56 (1951).

5. §701(e), 21 U.S.C. §371(e) sets up structured procedures for promulgating regulations for specified purposes. Regulations issued under six specified statutes require that any proposed regulations be published by the Secretary. Within 30 days, if objection is received, a public hearing will be held "for the purpose of receiving evidence relevant and material to the issues raised by such objections." The resulting regulations must contain detailed findings of fact and be based on substantial evidence in the record of the hearing. The original Act required that a hearing be held and a public record established before any regulations could be issued or amended. Later amendments allowed regulations meeting no opposition to be promulgated by this expedited mechanism. C. 143, 68 Stat. 55 (1954); c.861, §2, 70 Stat. 919 (1956); see Forte, Fair Hearing in Administrative Rule Making: A Recent Experience Under the Federal Food, Drug and Cosmetic and Fair Packaging and Labeling Acts, 1968 Duke L.J. 1, 11-17

Six portions of the Act to which the §701(e) procedures apply are: §401, 21 U.S.C. §341 (establishing definitional identity and quality standards for certain foods); §403(j), 21 U.S.C. §343(j) (labeling requirements for special dietary foods); §404(a), 21 U.S.C. §344 (a) (emergency permit control system); §406(a), 21 U.S.C. §346 (establishment of tolerances for poisonous ingredients in food); §502(d), 21 U.S.C. §352(d)(designation of habit forming drug derivatives); §502(h), 21 U.S.C. §352(h) (packaging requirements for certain drugs).

6. Plaintiffs argue that §701(a) regulations are "interpretative" in the sense that they are promulgated without statutory authority and thus lack the force of law. This court accepts with alacrity the authoritative view that it is not profitable to explore the asserted distinction, Toilet Goods Association v. Gardner, 360 F.2d 677, 686 (2d Cir. 1966), aff'd, 387 U.S. 167 (1967), which is "fuzzy at best." Shapiro, The Choice of Rulemaking or Adjudication in the Development of Administrative Policy, 78 Harv. L. Rev. 921, 930, 959-60 (1965). However labeled, the questioned regulations merit the respect owed an expert agency. See Skidmore v. Swift & Company, 323 U.S. 134, 136-40 (1944). No label can justify the claims, hereinafter considered, that the court should hear and determine these problems of medical and pharmacological judgment de novo.

7. "The agency has promulgated a substantial number of rules under §701(a)." Hamilton, Rulemaking on a Record by the Food and Drug Administration, 50 Texas L. Rev. 1132, 1133 n. 10 (1972). Among such regulations of clearly substantive proportions are those governing food nutritional labeling, 21 C.F.R. §1.17 (1973), information panel labeling requirements, 21 C.F. R. §1.8(d)(1973), food fat labeling, 21 C.F.R. §1.18 (1973), specifications of the identity of products which may be sold under specific common or usual names, 21 C.F.R. §102.1-8 (1973), Good Manufacturing Practice Regulations, 21 C.F.R. §128 (1973), and the extensive series of review mechanisms encompassing the Over-The-Counter drug review program, 21 C.F.R. §130.301 (1973).

Wisconsin District Judge James E. Doyle has determined that the Good Manufacturing Practice Regulations specifying standards for "insanitary conditions," 21 C.F.R. 128(a)(A), promulgated under 701(a) are "not to be given automatic and decisive effect" in a criminal proceeding under 21 U.S.C. §331(a). United States v. Everett Fisheries, Inc., No. 72-Cr.-109 (W.D. Wisc. May 30, 1973). Unlike the instant case, Everett was a criminal prosecution. The statutory language allegedly violated through the violation

Footnote 7 cont'd

of the regulation was open to a variety of meanings and thus open to interpretation and argument. Cf. Pendergast and McMurray, The Constitutionality of the Good Manufacturing Practices Provision of the Federal Food, Drug & Cosmetic Act, 23 Bus. Lawyer 445, 449-55 (1968); Barnard, Good Manufacturing Practices Regulations in the Food Industry, 22 Food Drug Cosm. L.J. 511, 513-14 (1967). It is also noteworthy that Judge Doyle's decision antedated Weinberger v. Hynson, Westcott & Dunning, considered just below in the text.

8. The words were quoted, at p. 620, from FPC v. Texaco, 377 U.S. 33, 39 (1964), as stating a governing principle.

A 202 Affidavit of Personal Service of Papers H LUTZ APPELLATE PRINTERS INC.

U.S. COURT OF APPEALS:SECOND CIRCUIT

Index No.

THE NATIONAL NUTRITUONAL FOODS ASSOCIATION, and SOLGAR, CO., INC.,
Plaintiffs-Appellants,
against
CASPER W. WEINBERGER, Secretary of Health, Education and Welfare and ALEXANDER M. SCHMIDT, Commissioner of Food and Drugs,
Defendants-Appellees.

Affidavit of Personal Service

STATE OF NEW YORK, COUNTY OF NEW YORK ss.:

I, James Steele, being duly sworn,

deposes and says that deponent is not a party to the action, is over 18 years of age and resides at

250 West 146th Street, New York, New York

That on the 5th day of August 1974 at U.S. Court House, Foley Square, N.Y.

deponent served the annexed Joint Appendix upon

Paul J. Curran-U.S. Attorney for the Southerd Dist.-Attorney for Defendants-Appellees

the in this action by delivering a true copy thereof to said individual personally. Deponent knew the person so served to be the person mentioned and described in said papers as the Attorney(s) herein,

James Steele

Print name beneath signature

Sworn to before me, this 5th day of August 1974

Robert T. Brin

JAMES STEELE

ROBERT T. BRIN
NOTARY PUBLIC, STATE OF NEW YORK
NO. 31 - 0413950
QUALIFIED IN NEW YORK COUNTY
COMMISSION EXPIRES MARCH 30, 1975